EXTRAMEDULLARY PLASMACYTOMA *

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Plasmacytoma, or plasmoma, was mentioned by Unna in 1891 and first described by Schridde in 1905. It is a tumor composed almost exclusively of plasma cells arranged in clusters or sheets with a scant, delicate, supportive, connective tissue stroma. Plasma cell tumors are divided into four groups: (1) myelomatosis or multiple myeloma, (2) solitary myeloma of bone, (3) plasma cell leukemia, and (4) extramedullary plasmacytoma.

In spite of several recent reports, extramedullary plasmacytomas are comparatively rare. Several pathologic conditions have been described under the term plasmacytoma, and there has been some duplication in reporting individual cases. However, a reasonable search through the literature reveals a total of 161 authentic cases of extramedullary plasmacytoma (Table I). The strange nature and behavior of this tumor, its relationship to the other groups of plasma cell tumors, and the unusual clinical features and long follow-up of one case (19 years) have stimulated us to undertake this study.

Extramedullary plasma cell tumors occur in a wide variety of organs and tissues. The majority of these are in the walls of the upper air passages. However, there is hardly an organ in which a plasma cell tumor or plasmacytoma has not been described.

TABLE I
Reported Cases of Extramedullary Plasmacytoma, Excluding the Conjunctiva

Upper respiratory tract and oral cavity	126
Other organs	35
Total	161

Hellwig, in 1943, analyzed 127 cases of extramedullary plasmacytoma. Stout and Kenny, in 1949 and covering the period between 1905 and 1949, did an exhaustive study of 104 cases with tumors in the upper air passages and oral cavity, including 9 of their own. These publications, as well as numerous others, form the basis for the present study. We have added a few cases not included in Hellwig's or Stout and Kenney's series up to 1949 and all those reported during the period between 1949 and 1953.

Table II summarizes, according to location, 22 additional cases of extramedullary plasmacytoma of the upper air passages and oral

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TABLE II

Summary of 22 Cases of Extramedullary Plasmacytoma of the Upper Air Passages and Oral Cavity, 1947 to 1956

Case	Site	Author and year	Age	Sex	Single	Multiple	Metastases		Duration before diagnosis	Course	Therapy	Remarks
							Lymph nodes	Other organs				
1	Nasopharynx	Waltner, 1947	38	M	+				25 yrs.	No recurrence in 2 yrs.		
2		Waltner, 1947	61	F	+			+	4 yrs.	No recurrence in 5 yrs., 8 mos.; died	Radiation	
3		Andersen, 1949	39	M	+		+		2 yrs.	Recurrence, died	Radiation	
4		Andersen, 1949	72	M	+				9 mos.	No recurrence	Surgery, radiation	
5		Andersen, 1949	77	F	+		+		1 yr.	Died 7 mos. later		
6		Rawson, 1950	53	M	+		+	+		Improvement for 9 mos.	Radiation, nitrogen mustard	
7		Fuerste, 1950	56	M		+		+		Died in 2 yrs.		
8		Dolin and Dewar, 1956	66	M	+				9 yrs.	Recurrence and symptom-free for 19 yrs.	Surgery, radiation	
9		Dolin and Dewar, 1956	65	M	+				3 mos.	Recurrence after 1 yr.	Radiation, surgery	

10	Nasal cavity	Andersen, 1949	73	F	+					No recurrence in 4 yrs.	Radiation	
11		Rawson, 1950	83	F	+				4 wks.	No recurrence in 2 yrs.	Radiation	
12		Rawson, 1950	73	M	+		+			Recurrence after 5 yrs., survival	Surgery, radiation	Recurred, treated by radiation
13		Rawson, 1950	72	M	+					No recurrence in 2 yrs.	Radiation	
14	Larynx	Bárány, (1937?)	73	M	+					1 yr. follow-up, no recurrence	Surgery	
15		Bárány, (1937?)	59	M	+					4 yrs., no recurrence		
16		Jaeger, 1942	74	M	+		+			3½ yrs.; died from intercurrent disease; no evidence of recurrence at necropsy	Radiation	
17		Rawson, 1950	59	M		+	+			10 yrs., 10 mos.; no recurrence		
18	Paranasal sinuses	Rawson, 1950	68	M	+				2 wks.		Radiation	No follow-up
19		Gupta, 1953	13	M	+				26 days		Radiation	No follow-up
20	Pharynx	Haines, 1942	75	M	+		+	+	9 mos.			No follow-up
21		Andersen, 1949	57	M	+				6 mos.	2 yrs., no recurrence	Surgery, radiation	
22	Palate	Gupta, 1953	80	F	+				8 mos.	2½ yrs.; died postoperatively from growth in maxilla	Surgery	

cavity in chronologic order as they appeared in the literature after 1947.

Table III summarizes, also in chronologic order, the cases of extramedullary plasmacytoma in organs other than the upper air passages and oral cavity published between 1909 and 1953.

Plasma cell tumors of the conjunctiva, another site of predilection for extramedullary plasmacytomas, are not included in this study. Forty-seven cases of plasmacytoma of the conjunctiva were cited by Hellwig. Details are scarce and the cases are difficult to evaluate. These tumors present a separate problem due to the controversy concerning their relationship to inflammatory processes, particularly trachoma, and the reader is referred to the ophthalmologic literature.

Report of Cases

Case 1

L. D. M. (U.H. no. 189–387), a white male, 66 years of age, was first seen at the University Hospitals on August 10, 1944. In 1935 he had noticed gradually increasing difficulty in breathing through his nose. He was told he had a "blood tumor," and "cancer paste" was applied to a mass in the nose. He was partially relieved of his symptoms. In July, 1941, he noticed swelling of the left ankle. The swelling increased gradually and a roentgenogram (Fig. 1) revealed an expanding, destructive lesion of the distal end of the tibia. On March 7, 1942, the tibial lesion was excised and the defect filled with bone grafts. Microscopic examination (Fig. 2) revealed a plasma cell tumor. Difficulty in breathing through the nose increased and on August 10, 1944, a brown-red tumor was noted, projecting from the nasal orifice, completely obstructing the nasal passages, and protruding posteriorly behind the uvula. The nasal bones and cartilage were destroyed, and the defect showed sharply demarcated edges, presumably the result of the "cancer paste." Biopsy of this tumor (Fig. 3) revealed a plasmacytoma.

The nasal tumor was treated by radiation: 2,400 r. in air to two fields in a period of 2 weeks. Ten weeks later, the nasal obstruction was relieved completely. However, there was still residual tumor present, and a second course of radiation therapy was given: 1,000 r. to two fields within a period of 1 week. When examined 6 months later, the oro-pharyngeal obstruction was relieved completely and no residual tumor was noted.

At that time the patient complained of pain and swelling in the left knee. A roentgenogram (Fig. 4) on September 11, 1945, revealed a destructive lesion invading the distal end of the femur. A mid-thigh amputation was performed. Microscopic examination again revealed a plasma cell tumor. The skeletal survey failed to reveal any other involvement.

Total serum proteins, albumin-globulin ratio, and all other laboratory tests were within normal limits. No Bence Jones protein was found. Five months later, the patient began to complain of pain and swelling in his right ankle. A roentgenogram revealed an expanding, rarefying lesion of the distal end of the right fibula. Repeated skeletal survey again failed to reveal other bone involvement. Laboratory tests, including those for Bence Jones proteinuria, were repeatedly negative. The lesion of the distal end of the right fibula was excised and the microscopic diagnosis was plasma cell tumor. The symptoms returned in the middle of 1951 and a recurrent plasma cell tumor of the distal end of the right fibula again was excised on February 27, 1952.

The patient was symptom-free until the end of 1952, when again he noted difficulty

TABLE III

Summary of 35 Cases of Extramedullary Plasmacytoma of Regions Other than the Upper Respiratory Area, 1909 to 1953

Case	Site	Author and year	Age	Sex	Single	Multiple	Metastases		Duration before diagnosis	Course	Therapy	Remarks
							Lymph nodes	Other organs				
1	Ileum	Vallone, 1930	24	M	+						Surgery	
2		North, 1930	47	F	+						Surgery	
3		Razzaboni, 1930				+					Surgery	
4		Brown and Liber, 1939	57	M		+	+	+	14 yrs.	Died post-operatively		Also colon
5		Arel, 1946	8	M	+				6 mos.	Died 17 days postoperatively	Surgery	
6	Lymph nodes	Maresch, 1909	48	M	+		+	+	18 yrs.	Died post-operatively	Surgery	
7		Jackson, Parker, and Bethea, 1931	67	F	+					3 yr. follow-up	Surgery	
8		Jackson, Parker, and Bethea, 1931	53	M		+		+		Few weeks, died; no necropsy		
9		Basset and Scapier, 1937	48	M	+			+	2 yrs.	6 mos., died postoperatively	Radiation, surgery	

TABLE III (continued)

Case	Site	Author and year	Age	Sex	Single	Multiple	Metastases		Duration before diagnosis	Course	Therapy	Remarks
							Lymph nodes	Other organs				
10	Stomach	Vasiliu and Popa, 1928				+	+					No details
11		Jaeger, 1942	45	F	+		+	+		4½ yrs., recurrence; 3½ yrs., no recurrence	Surgery, radiation	
12		Esposito and Stout, 1945	35	M		+	+		3 yrs.	2 yrs., died	Surgery, radiation	
13		Arel, 1946	15	M	+					Recurrence, died	Surgery, radiation	
14		Couret, 1946	48	F	+		+		8 yrs.	1 yr., died; recurrence	Surgery	
15		Schwander, Estes, and Cooper, 1947	42	M	+		+		6½ yrs.		Surgery	
16		Gupta, 1953	35	M	+					6 mos.	Surgery, radiation	
17	Lung	Gordon and Walker, 1944	30	F	+							
18		Rozsa and Frieman, 1953	69	M	+					11 mos., no symptoms	Surgery, radiation	
19	Thyroid gland	Voegt, 1938			+						Surgery	
20		Shaw and Smith, 1940	50	F	+					1 yr. follow-up, no recurrence	Surgery, radiation	

21	Submaxillary area	Aragona, 1936	6	F	+					5 yr. follow-up, no recurrence		
22		Andersen, 1949	52	F	+					3½ yrs., no recurrence	Radiation, surgery	
23	Pleura	Klose, 1911	61	M	+					Died post-operatively	Surgery	
24	Mediastinum	Bross, 1931	54	M	+						Surgery	
25	Scalp	Wright, 1953	50	M	+							
26	Skin	Hedinger, 1911	48	F	+		+		40 yrs.(?)		Surgery	
27	Spermatic cord	Ciaccio, 1913	38	M	+				2½ yrs.	8 yrs.	Surgery	
28	Vulva	Martinotti, 1910										Cited by Hellwig
29	Vagina	Appleberg, 1953		F	+					No recurrence	Surgery	
30	Breast	Cutler, 1934	49	F		+	+			20 mos.	Surgery, radiation	
31	Kidney	Knudsen, 1937			+					1 mo. follow-up, no recurrence		
32	Lacrimal gland	Parker, 1937	66	F	+					2 recurrences in 16 mo. follow-up	Surgery, radiation	Eroded maxillary bone
33	Ovary	Voegt, 1938	30	F	+						Surgery	
34	Cervix	Andersen, 1949	34	F	+	+			2 mos.	3½ yrs., no symptoms	Radiation	
35	Testicle	Andersen, 1949	72	M	+				2 mos.		Surgery, radiation	

in breathing through his nose. A recurrent red-brown nasopharyngeal tumor was found blocking the nasal passages. A biopsy of the tumor (Fig. 5) revealed plasmacytoma.

Another course of radiation therapy was administered: 2,000 r. in air to one field, 6 by 8 cm., within a period of 3 weeks. Skeletal survey again was negative. Total serum proteins, 8.3 gm. per 100 ml.; albumin-globulin ratio, 5.4/2.9. Electrophoretic determinations were normal. Serum calcium was 11 mg. per cent; serum phosphorus, 2.7 mg. per cent; serum alkaline phosphatase was within normal limits. No Bence Jones protein was found.

The patient was last seen on July 1, 1953. Examination revealed complete regression of the nasopharyngeal mass. Small, localized, indurated areas were noted in the nasal passages. Biopsy of an indurated area failed to show the presence of plasma cells. Results of laboratory tests were again within normal limits. A skeletal survey remained negative.

Case 2

A 65-year-old white male (U.H. no. 215–749) was admitted to the University Hospitals on July 9, 1953. He had noticed a nasal discharge 15 months before admission. Three months after admission, a tumor was found above the hard palate and biopsy showed it to be a plasmacytoma (Fig. 6). Radium needles were implanted, and this was repeated in October, 1953. The patient had no complaints until February, 1954, when he noticed an ulcer over his palate and burning pain ensued.

On admission, an ulcer through the hard palate, measuring 2 by 3 cm., was found. The defect exhibited folded, gray edges. Biopsy revealed recurrent plasmacytoma and osteonecrosis of the hard palate. Radical excision was performed. Laboratory tests including those for Bence Jones protein and serum proteins and a skeletal survey were negative. The patient is being followed currently.

Distribution and Location

Haines, in a comprehensive study of malignant tumors of the upper air passages at Westminster Hospital, found that 50 to 90 per cent were epithelial tumors, the remainder being in the lymphosarcoma group. Plasma cell tumors were mentioned only occasionally by this author. Jaeger found 0.5 per cent of the malignant tumors of the upper air passages and oral cavity on file at the Roentgen Institute in Zurich to be plasmacytomas. It is evident that plasma cell tumors represent a rather small but nevertheless important fraction of the malignant tumors of the upper respiratory passages and oral cavity, and that hitherto they either have been confused with, or included in, the group of lymphosarcomas. Of all extramedullary plasmacytomas, 78.1 per cent occur in the upper air passages and oral cavity.

The distribution of plasmacytomas according to age and sex varies. Gormsen found 82 per cent in males between the ages of 40 and 70. Stout and Kenney found 80 per cent in males and the age distribution to be 10 to 89 years. An analysis of our tables reveals that 85 cases of extramedullary plasmacytoma of the upper air passages and oral cavity occurred in males, 22 in females, and in 19 cases the sex was not reported. This again reveals a 79.4 per cent preponderance for the male sex.

Of the 35 cases of extramedullary plasmacytoma in organs other than the upper air passages and oral cavity, 16 occurred in males and 14 in females. In 5 cases the sex was not reported. The age distribution ranged from 6 to 72 years.

Table IV presents the distribution of plasmacytomas of the upper air passages and oral cavity according to their location and site of metastases. This table indicates that 38 of the 126 cases metastasized to regional lymph nodes and/or to distant organs.

It is worthy of note that only 12 of the 113 cases, in respect to which this information was known, had multiple lesions (10.6 per cent). Only 2 of those had metastases. These figures vary slightly from those published by Andersen and approach closely those given by Stout and Kenney. It was found that metastases may occur to distant organs, bone, and skin without involving regional lymph nodes, and that regional lymph node involvement does not necessarily imply a bad

TABLE IV

Location and Distribution of Plasmacytomas of the Upper Air Passages and Oral Cavity

Site	Number	Single focus	Multiple foci	Single or multiple undetermined	Metastasis		
					Lymph nodes	Bones	Other organs
Nasal cavity	28	24	4		9	3	3
Nasopharynx	29	23	5	1	4	3	1
Paranasal sinuses	16	14		2	4	2	1
Tonsils	15	14		1	8	4	
Maxilla and gingiva	8	7	1				
Pharynx	7	6		1	3		
Palate	5	5			1		
Epiglottis and subglottis	5	4	1		2	1	2
Floor of mouth	2	2					
Posterior pillar	1		1				
Uvula	1	1					
Tongue	1	1					
"Nasal and paranasal sinuses" (Geschickter)	8			8			
Total	126	101	12	13			

prognosis. The tumor may be limited or localized to the regional lymph nodes in a large number of cases. Although the number of our cases is not great, the pattern of behavior is usually the same, and our findings concur with the views of many other investigators.

Table V presents the distribution of extramedullary plasmacytomas in organs other than the upper respiratory passages and oral cavity,

and shows their sites of metastases. In this group, 27 tumors were single, 6 were multiple, and 2 were undetermined in this respect. Eleven (31.4 per cent) of the 35 had metastasized to regional lymph nodes and/or distant organs. The majority of these, 7 cases (64 per cent), showed metastases to regional nodes only. Five (46 per cent) of the 11 cases with metastases had multiple lesions. Six (54 per cent) were single. Thus, 31.4 per cent of the plasmacytomas of other organs metastasized as compared to 30.1 per cent of the plasmacytomas of the upper air passages.

TABLE V

Distribution of Metastases in Extramedullary Plasmacytoma of Other Regions Than Upper Respiratory Tract and Oral Cavity

Site	Number of cases	Single focus	Multiple foci	Metastasis	Metastasis			Remarks
					Lymph nodes	Bones	Other organs	
Ileum	5	3	2	1	1		1	
Lymph nodes	4	3	1	3	1		3	
Stomach	3	2	1	3	3			
Cecum	3	3		1	1		1	
Submaxillary area	2	2						
Lung	2	2						
Thyroid gland	2	2						
Jejunum	1		1	1	1			
Pleura	1	1						
Mediastinum	1	1						
Skull	1	1			1			
Skin	1	1		1				
Spermatic cord	1	1						No details
Vulva	1							
Vagina	1	1		1				
Breast	1		1		1			
Kidney	1	1						
Lacrimal gland	1	1						
Ovary	1	1						
Cervix	1	?	?					
Testicle	1	1						
Total	35	27	6	11*				

* Six single, 5 multiple.

SURVIVAL AND FOLLOW-UP

A careful analysis of the literature reveals scarcity of details and lack of accuracy in a great number of the reports. Of the 126 cases of plasmacytoma of the upper air passages and oral cavity, 44 were not

accurately described or followed. Hence, our analysis is limited to 82 cases.

Table VI shows the follow-up and survival of patients with plasmacytomas of the upper air passages and oral cavity. Of the 61 cases followed for not more than 4 years, the distribution as to status at time of follow-up and the percentage of the total 82 cases represented by each subgroup appears in Table VI. Of the 7 alive with evidences of the neoplasm, 5 had recurrence at the original site and 2 had metastases to bones. Of the 24 who had died from plasmacytoma in 4 years, 2 succumbed postoperatively and only one of the 24 showed evidence of metastases to distant organs. In the second line of Table VI a similar distribution is shown for the cases which were followed for the period of 5 to 10 years after onset.

In the literature, cases were reported which were followed for more than 10 years and a few of these require special mention. Rawson followed a case for 11 years and 10 months without evidence of recurrence or metastasis. Von Werdt, Wachter, Oppikofer, and Claiborn and Ferris followed cases for periods of 10½ to 14 years without any evidence of recurrence or metastasis. Piney and Riach followed a patient for 12 years, who then developed metastases to bones and died 1 year later. Jaeger followed a case for 25 years. This patient had four local

TABLE VI

Survival Rate of Patients with Plasmacytoma of the Upper Air Passages and Oral Cavity

	Number of cases	Alive, free of symptoms	Alive, with symptoms	Died from plasmacytoma	Died from intercurrent disease
1–4 years	61	22 cases (26.8%)*	7 cases (8.5%)	24 cases (29.3%)	8 cases (9.8%)
5–10 years or more	21	12 cases (14.6%)	4 cases (4.9%)	5 cases (6.1%)	
Not followed	44				
Total	126				

* All percentages refer to the 82 cases which were followed.

recurrences and multiple bone involvement, yet he was still alive and symptom-free. Figi, Broders, and Havens followed 2 cases for 12½ and 16 years, respectively, without evidence of disease. Stout and Kenney followed a case for 14½ years without evidence of recurrent disease. One of our cases had been followed for 19 years.

In Table VII are summarized the follow-up and survival data in 35 cases of extramedullary plasmacytoma of organs other than the upper air passages and oral cavity. Eight cases lacked details and follow-ups, so that only 27 could be evaluated properly. Therefore all percentages

are based on the 27 cases which were followed and the results appear in Table VII. Five of the 8 patients who died from plasmacytoma succumbed during or shortly after operation.

A comparison of Tables VI and VII indicates that the percentage of the patients alive and free of disease in the period of 1 to 4 years is greater in plasmacytomas of other organs than in those of the upper air passages and oral cavity, 48.1 per cent versus 26.8 per cent. However, this ratio is reversed, or actually close to unity (11.1 per cent versus 14.6 per cent) as the longer follow-up period of 5 to 10 years is reached. Combination of Tables VI and VII indicates the survival rate of 109 cases of extramedullary plasmacytoma. Of 82 patients followed for 1 to 4 years, 35 were alive and free of disease (42.7 per cent). Of 27 patients followed for 5 to 10 or more years, 15 were alive and free of disease (55.6 per cent).

TABLE VII

Survival Rate of Patients with Plasmacytomas of Other Organs than Upper Air Passages and Oral Cavity

	Number of cases	Alive, free of symptoms	Alive, with symptoms	Died from plasmacytoma	Died from intercurrent disease
1–4 years	21	13 cases (48.1%)*		8 cases (29.7%)	
5–10 years or more	6	3 cases (11.1%)	3 cases (11.1%)		
Not followed	8				
Total	35				

* All percentages are based on the 27 cases which were followed.

DISCUSSION AND CONCLUSIONS

Extramedullary plasmacytomas vary considerably in size, the diameter ranging from one to several centimeters. They usually are well limited, firm, and spherical, but they may be lobulated, pedunculated, or polypoid and show evidence of infiltration. The great majority are yellow-gray with a red cut surface, while some of the tumors have a blue-red appearance. Involved regional lymph nodes are firm, gray-white, and may measure up to 3 cm. The symptoms are those due to pressure and obstruction. The nasal cavity or nasopharynx may be obstructed completely; a feeling of fullness of the sinuses is a frequent symptom when the tumor involves them. In the gastrointestinal tract, obstruction is the predominant feature of the clinical picture. Bleeding is a frequent accompaniment and many of the tumors show ulceration. The clinical course is extremely variable. As to behavior, these tumors fall into several main categories: (1) Tumors which are solitary;

(2) Tumors which are infiltrative and destroy adjacent tissue; (3) Tumors which are prone to recur after inadequate removal or inadequate radiation therapy; (4) Tumors which, as a group, show regional lymph node metastases; (5) Tumors which metastasize to adjacent lymph nodes and other organs; (6) A solitary tumor in soft tissues, with one or more tumors in other organs, usually bones.

Microscopic Appearance

Marschalkó, in 1895, described the principal component of the plasmacytoma as a plasma cell. To the plasma cell he assigned four distinct characteristics, as follows: (1) The cells are round, oval, or polygonal with abundant basophilic cytoplasm. Inclusions are not distinct or constant and Russell bodies are not found. (2) The nucleus is distinctive, being eccentrically placed. (3) A paranuclear halo is present. (4) A small nucleus has five to eight deeply stained clumps of chromatin radially arranged at the nuclear membrane. It is this characteristic that suggested the term cartwheel nucleus. Actually, one does not always find these distinctive characteristics clearly drawn. The cells may show considerable atypism and variation in size. The radial clumps of chromatin in the nuclei are not always apparent. In many instances numerous mitotic figures are noted.

All investigators agree that there should be no difficulty in distinguishing true plasma cell neoplasms from plasma cell granulomas (Voegt; Jaeger; Stout and Kenney). A granuloma shows a variety of cells; there is a mixture of plasma cells, leukocytes, lymphocytes, and fibroblasts. Macrophages usually are present and there is a proliferation of blood vessels throughout the granulomatous structure. Many of the "plasmacytomas" of the conjunctiva would fall under this category, according to Chojnacki. A true plasma cell neoplasm, on the other hand, is composed of compact clusters or sheets of plasma cells with very little connective tissue stroma.

Hellwig believed that the more atypical the plasma cell, the greater the variation in its size, and the more mitotic figures present, the higher the degree of malignancy. Ringertz suggested that a more delicate reticular stroma would indicate a more rapidly growing and metastasizing tumor. He did not accept a close relationship between the relative maturity of the plasma cells and their behavior. It has been stressed by various authors that the microscopic appearance need not be an indication of behavior. According to Boyd, plasma cells of all types are but variations of one cell type, and the apparent variety is due merely to anaplastic changes in that one fundamental type. As to the origin of the plasma cell, Maximow, in 1928, considered that it is de-

rived from the lymphocyte and, accordingly, to him plasma cell tumors were simply a variety of lymphomas.

Klemperer and Rohr believed that the plasma cell is an abnormal hematic cell, the origin of which may be traced to the primitive reticulum cell of the bone marrow. Hayes concluded that neoplastic plasma cells are immature plasmacytes derived from reticulo-endothelial cells. Jaeger stated that extramedullary plasmacytomas arise from plasma cells in lymphatic tissue, while plasmacytomas of bone arise from plasma cells of the osseous medulla. Lymph node involvement in multiple myeloma is exceedingly rare, while lymph node involvement in extramedullary plasmacytoma is almost the rule. Most pathologists share the view that multiple myelomatosis is a generalized disease and that metastasis plays no part in its development.

Although there is far from universal agreement on the origin and nature of the plasma cell, most authors follow Maximow in accepting a close relationship between the plasma cell and the lymphocyte.

The behavior and the clinical picture of extramedullary plasmacytoma, in contrast to multiple myelomatosis or plasma cell leukemia, favor Jaeger's views in dividing those entities regardless of whether all plasma cells have the primitive lymphocyte as their mother cell. Autochthonous growth in extramedullary locations is the most probable explanation. Plasma cell leukemias appear to present an exaggeration of all the phenomena of multiple myelomatosis (Breitenbucher and Hertzog).

The plasma cells found in multiple myelomatosis may have the same appearance as those of extramedullary plasmacytoma, or may actually be the same cells. However, in multiple myelomatosis they are part of a generalized widespread systemic disease with a disturbance in protein metabolism. Magnus-Levy emphasized the close relationship between plasma cells and the formation of serum proteins. Smereker believed that in multiple myelomatosis the metabolic disturbance is influenced by a neurosecretory mechanism in the pathways between the hypothalamus and the neurohypophysis. Jeschal likewise considered that the changes in the form of crystal pods or basophilic staining of the plasma cells are associated with abnormal protein formation. Brasz pointed to the laying down of abnormal proteins—paraproteins—in the form of crystals in the reticulum cells of the bone marrow in multiple myelomatosis. Extramedullary plasmacytomas do not exhibit the manifestations of this disturbance in protein metabolism. From these facts the impression may be gained that extramedullary plasmacytoma can be considered as a separate, distinct entity. The term

extramedullary plasmacytoma should be applied only to cases in which disseminated myelomatosis can be ruled out by roentgenologic, hematologic, chemical, and morphologic investigations (Bichel and Kirketerp, and others).

A precocious lesion of multiple myelomatosis may appear to be solitary for some months. A number of authors have stressed the fact (Lumb, Willis) that plasma cell tumors commencing in a solitary form may subsequently become multiple myelomatosis. This is true for some cases of solitary myeloma of bone and for some cases of extramedullary plasmacytoma. The study of solitary myeloma of bone and its relationship to multiple myelomatosis is beyond the scope of this paper. However, as far as the extramedullary plasmacytomas are concerned, it is our opinion, after a careful study of 161 cases, that this possible relationship to systemic disease should not alter the idea of separating these entities.

Obviously, one may encounter great difficulty in classifying a case of extramedullary plasmacytoma exhibiting multiple metastases to bones. The clinical picture may resemble multiple myeloma. However, the plasma cells of the bone marrow do not take part in a widespread involvement and the signs of disturbance in protein metabolism are not manifest. Caution must likewise be taken in the evaluation of cases of multiple myelomatosis with occasional involvement of extramedullary soft tissues (Hayes).

Most authorities agree that the clinical picture rather than the microscopic appearance should form the final basis for the evaluation of extramedullary plasmacytoma as such. Once the histopathologic nature of the extramedullary tumor has been established, one should explore the possibility that it merely represents the first manifestation of multiple myelomatosis. Tests for Bence Jones proteinuria; determination of total serum proteins, and of the albumin-globulin ratio, including electrophoretic curves; bone marrow aspiration, and roentgenologic survey of the skeleton should constitute the essential parts of the clinical investigation. Only after all of these tests have been evaluated and have been found negative as to multiple myeloma, and the patient followed closely for a period of 1 to 2 years, may one classify a tumor as an extramedullary plasmacytoma. These tumors may fall into one of the previously mentioned six clinical groups. Extramedullary plasmacytomas sometimes are permanently cured by surgical excision or radiation therapy. On the other hand, the prognosis in multiple myelomatosis is extremely poor; the average survival is 2 to 3 years.

Our analysis of 161 cases of extramedullary plasmacytoma published in the literature from 1905 to 1953 reveals that of 109 which were followed, 50 patients were alive and symptom-free for a period of 1 to 10 years or more, thus indicating a survival rate of 45.9 per cent.

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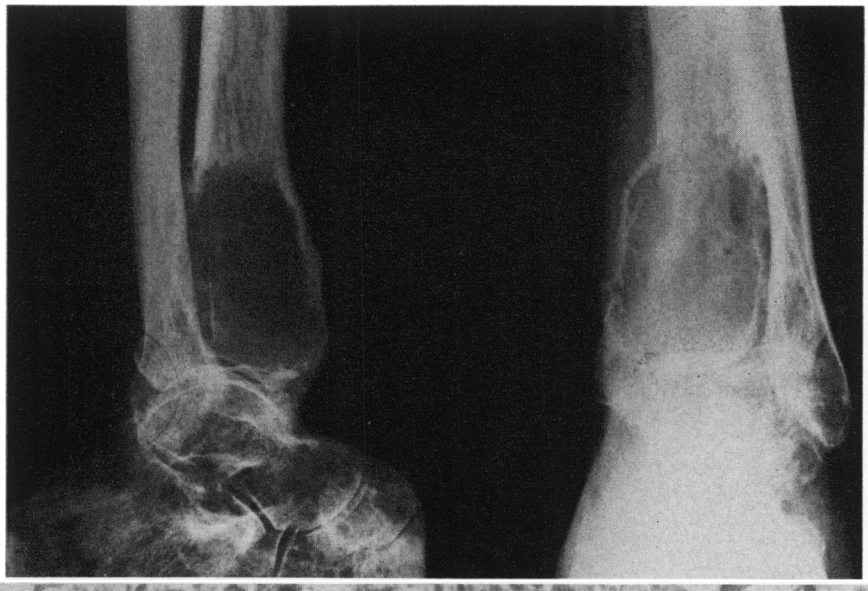
LEGENDS FOR FIGURES

FIG. 1. Case 1. Roentgenogram of the left ankle. There is a large, destructive tumor at the distal end of the tibia with expansion and break-through of the cortex at the medial aspect and invasion of the soft tissues.

FIG. 2. Case 1. Photomicrograph of the tumor of the distal end of the tibia. Sheets and cords of cells with abundant cytoplasm and eccentric nuclei are shown. Most of the nuclei show "cartwheel" clumping of the chromatin. Some of the nuclei are dense.



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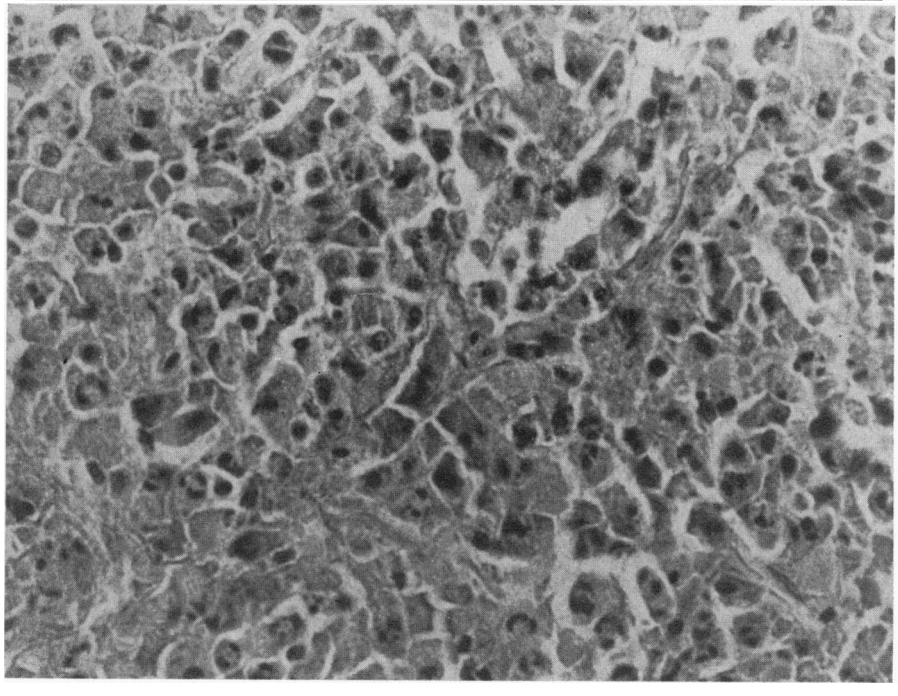

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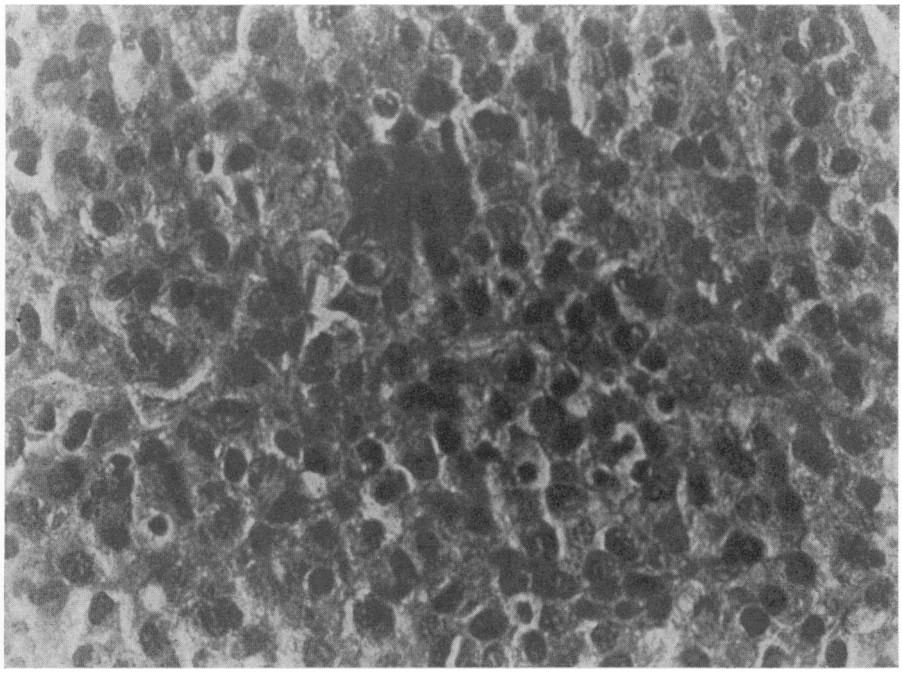

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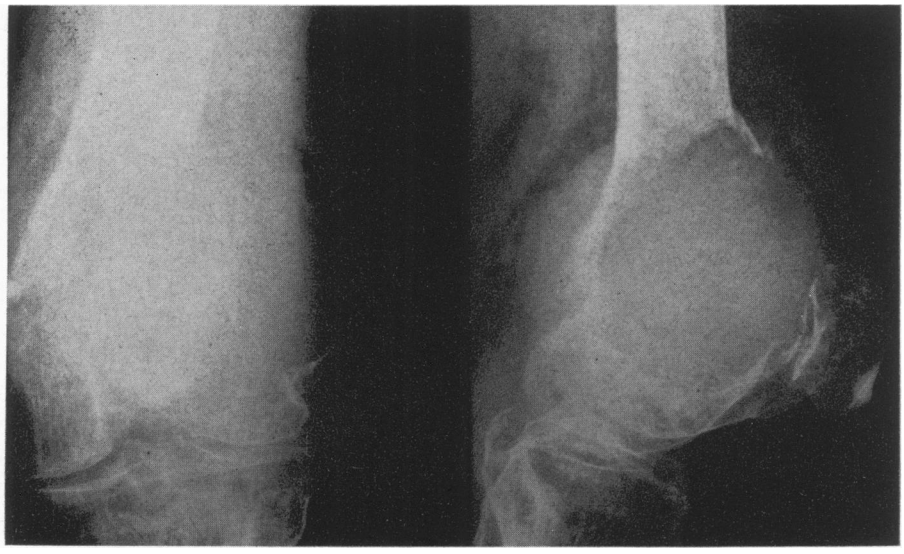
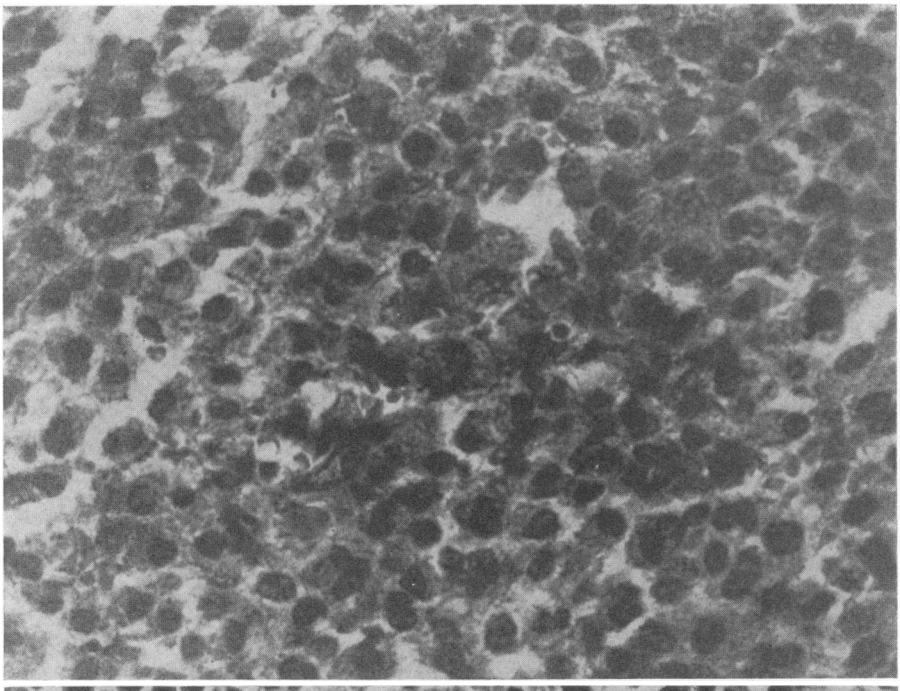


FIG. 3. Case 1. Photomicrograph of the nasopharyngeal tumor. Sheets and cords of cells with abundant cytoplasm and eccentric nuclei are demonstrated. Most of the nuclei are dense and hyperchromatic. Some of the nuclei show the "cart-wheel" clumping of the chromatin.

FIG. 4. Case 1. Roentgenogram of the left knee. An extensive destructive lesion is present at the distal end of the femur with a break in the cortex and invasion of the soft tissues at the lateral and posterior aspect.



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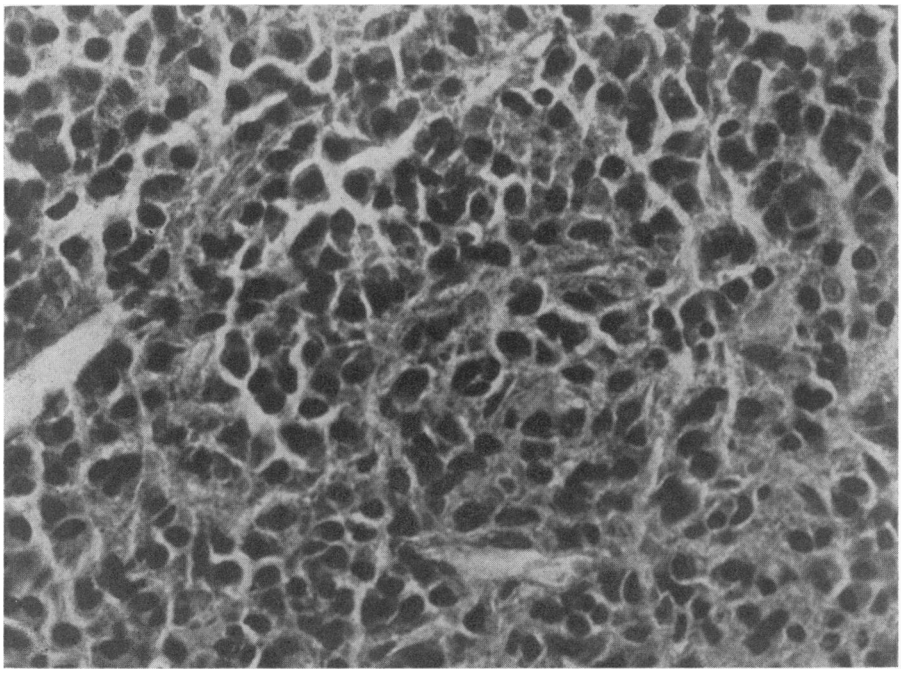

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FIG. 5. Case 1. Photomicrograph of the nasopharyngeal recurrent tumor. The recurrent tumor shows a microscopic pattern similar to the original specimen (cf Fig. 3).

FIG. 6. Case 2. Photomicrograph of the nasopharyngeal tumor. Sheets and cords of cells with abundant cytoplasm and eccentric nuclei are present. Some of these are adjacent to small blood vessels. Most of the nuclei are dense and hyperchromatic.