A Histopathological and Immunohistochemical Study of Vascular Localization on Schwannoma in the Oro-maxillofacial Region

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Abstract

Schwannoma is a relatively rare, benign peripheral nerve sheath tumor that affects the oro-maxillofacial region. The peripheral nerve tissues are known to be closely related to vascular tissues from viewpoints of morphology and physiology. Therefore, the authors speculate that schwannoma of peripheral nerve origin is also associated with vascular tissues ; however, the histogenesis with regard to vasculature is not fully understood. The authors investigated the localization of the blood and lymphatic vessels in schwannoma using histopathological and immunohistochemical methodologies. The tumor parenchyma consisted of a proliferation of relatively long spindle cells with nuclear palisading (Antoni A type), diffuse spreading with myxoid or edematous background (Antoni B type), and encapsulation with fibrous tissue (capsular tissue). In one case, the tumor exhibited multicystic growth. Dilation and hyperplasia of the vessels were observed in the Antoni A and B zones, the border of the Antoni A and B zones (border zone), and capsular tissue. With periodic acid-Schiff reaction-alcian blue pH2.5 staining, the myxoid matrix in the Antoni B zone was stained blue. Immunohistochemically, CD-34-positive blood vessels were found in all cases. The vessels were predominantly observed in the Antoni B zone, and only moderately in the Antoni A zone, border zone, and capsular tissue. Four cases showed that D2-40-positive lymphatic vessels were mainly observed in the Antoni B zone and capsular tissue, and only moderately in the Antoni A zone. In the other four cases, D2-40-positive lymphatic vessels were only indicated in the capsular tissue. In addition, positive immunoreactivity for D2-40 was found in the cyst-lining cells in the multicystic case. Microvessel density (MVD, numbers of blood vessels per unit area) was calculated for CD-34-positive blood vessels. MVD was 3.4 ± 2.1 in the Antoni A zone, 6.0 ± 1.7 in the border zone, 9.4 ± 3.2 in the Antoni B zone, and 2.7 ± 1.0 in the capsular tissue. In addition, lymphatic vessel density (LVD, numbers of lymphatic vessels per unit area) was calculated for D2-40-positive vessels. LVD was 0.2 ± 0.5 in the Antoni A zone, 2.7 ± 3.5 in the Antoni B zone, and 2.4 ± 0.9 in the capsular tissue. These results suggest that the localization of the blood and lymphatic vessels was closely associated with the histogenesis of the Antoni B zone in schwannoma, not only by the degeneration and over-expression of the myxoid matrix but also by the edematous change from circulation disturbance in the tumor tissues during benign tumor growth and development.

Keywords :

schwannoma, lymphatic vessels, blood vessels, immunohistochemistry

Introduction

Schwannoma is a relatively rare benign tumor in the oro-maxillofacial region, although the tumor has

been well studied in the field of soft tissue tumor pathology (1-3). Histogenetically, the parenchyma is derived from peripheral neural organs associated

with Schwann cells. In addition, peripheral nerve tissues are known to be closely related to vascular tissues from viewpoints of morphology and physiology (4). Therefore, schwannoma of peripheral nerve origin is also speculated to be associated with vascular tissues; however, the histogenesis with regard to vasculature is not fully understood.

Several immunohistochemical markers of endothelial cells of the blood and lymphatic vessels have been used in histopathological studies, such as anti-CD34 (5, 6) and anti-podoplanin (7, 8) antibodies, and the studies have provided information about the biological behavior of vascular tumors and the vascular invasion of malignant tumors. The immunohistochemical localization of marker expression is thought to be a useful method for observing vascular formation in schwannoma.

The localization of the blood and lymphatic vessels in schwannoma using histopathological and immunohistochemical methodologies was investigated to elicit additional knowledge of the histopathological and immunohistochemical characteristics in oro-maxillofacial schwannoma in the present study.

Materials and methods

Materials

Eight cases of schwannoma, definitively diagnosed at the Department of Oral Pathology, Nihon University School of Dentistry at Matsudo, were used for the present study. Consideration was given to patient privacy, diagnosis, and the management and prognosis of the lesion (Ethics committee recognition number: EC 10-005).

Methods

The extirpated specimens were immediately fixed in 10% neutral formalin solution and then made into paraffin-embedded blocks, which were sectioned at a thickness of 4 μ m for histopathological observation. The sections were stained with hematoxylin-eosin staining (HE) and periodic acid-Schiff reaction-alcian blue pH2.5 staining (PAS-AB) after deparaffinization.

Envision polymer+ kit (DakoCytomation, Glostrup, Denmark)

was used for the immunohistochemical study. The paraffin sections were deparaffinized, dehydrated, and incubated in 0.01 M phosphate buffer, at 120 °C for 10 min, for antigen retrieval. Monoclonal anti-S-100 β protein (S-100 β) (DakoCytomation, Glostrup, Denmark), monoclonal anti-CD34 (CD34) (DakoCytomation, Glostrup, Denmark), and monoclonal anti-podoplanin (D2-40) (Nichirei, Tokyo, Japan) were used as primary antibodies. The sections were incubated with the antibodies for 60 min at room temperature. The peroxidase activity was visualized using diaminobenzidine.

Positive control tests were performed on healthy peripheral nerve tissues, the blood and lymph vessels from the tumor tissue specimens, and healthy oral mucosa. For negative control testing, samples were incubated with mouse IgG instead of primary antibodies; no staining reactions were obtained. Finally, the immunohistochemical sections were counterstained with Mayer's hematoxylin.

In addition, microvessel density (MVD, numbers of blood vessels per unit area) and lymphatic vessel density (LVD, numbers of lymphatic vessels per unit area) were counted for quantitative analysis of the distribution of the blood and lymphatic vessels in the present study in accordance with previous studies (9, 10). Sections were first examined at low magnification ($\times 100$) to identify areas with the most intense staining and highest apparent density of CD-34-positive microvessels (MVD) and D2-40-positive lymphatic vessels (LVD) (hot spots). Three areas of hot spots were selected and the slides for MVD and LVD counting were independently evaluated using high magnification ($\times 400$) (unit area, 0.15 mm²). The data are indicated as mean $\pm$ S.D.

The significant difference was statistically analyzed with Tukey-Kramer's test and the significance level was set at $p < 0.05$.

Results

Clinical findings

The present study examined eight cases of schwannoma. The patient age ranged from 5 to 58 years

(mean, 27.9 years) and the male-to-female ratio was 5 : 3. The sites of occurrence were the tongue (two cases, 25%), neck (two cases, 25%), gingiva (one case, 12.5%), palate (one case, 12.5%), floor of the mouth (one case, 12.5%) and the parotid region (one case, 12.5%). Among these cases, seven showed solid tumors ; only one case indicated a multicystic tumor.

Histopathological findings

The tumor parenchyma consisted of a proliferation of relatively long spindle cells with eccentric, slender nuclei and encapsulated fibrous tissue (capsular tissue). The parenchyma consisted of two parts (Fig. 1a) : an arrangement in epithelium-like sheets and nest formation with nuclear palisading, which corresponded to the Antoni A type ; and diffuse spreading with myxoid or edematous background, which corresponded to the Antoni B type (1-3). In one of the eight cases, the tumor exhibited multicystic growth (Fig. 1b). Various sized vessels with dilation and hyperplasia were observed in the areas of the Antoni A zone (Fig. 1c), the Antoni B zone (Fig. 1d), and the border of the Antoni A and B zones (border zone) (Fig. 1e) with a minimal level of inflammatory cell infiltration. No malignant features, such as cellular or structural atypism and invasive growth, were evident. The tumor parenchyma was encapsulated with fibrous tissues. With PAS-AB staining, the myxoid matrix in the Antoni B zone was stained blue (Fig. 1f).

Immunohistochemical findings

Positive immunoreactivity for S-100 β (Fig. 2a) was observed in the tumor cells. Positive reactivity for CD34 was indicated in the endothelial cells of the blood vessels in the Antoni A zone (Fig. 2b, c), border zone (Fig. 2b, d), Antoni B zone (Fig. 2b, e), and capsular tissue in all cases. The positive vessels were found around cystic spaces in the multicystic case (Fig. 2f). Positive immunoreactivity for D2-40 was observed in the endothelial cells of lymphatic vessels. The positive vessels were mainly localized in the capsular tissue and Antoni B zone, and moderately in the Antoni A zone in four cases (Fig. 3a, b). The other

four cases showed D2-40-positive lymphatic vessels only in the capsular tissue. Positive immunoreactivity was also found in the cyst-lining cells in the multicystic tumor (Fig. 3c).

MVD (numbers of CD34-positive blood vessels per unit area (0.15 mm²)) and LVD (numbers of D2-40-positive lymphatic vessels per unit area (0.15 mm²)) are shown in Fig. 4.

MVD was 3.4 ± 2.1 in the Antoni A zone, 6.0 ± 1.7 in the border zone, 9.4 ± 3.2 in the Antoni B zone, and 2.7 ± 1.0 in the capsular tissue. Significant differences in MVD were shown between the Antoni A and Antoni B zones, and between the Antoni B zone and capsular tissue ($p < 0.05$) (Fig. 4a). Lymphatic vessel density was 0.2 ± 0.5 in the Antoni A zone, 2.7 ± 3.5 in the Antoni B zone, and 2.4 ± 0.9 in the capsular tissue. No significant differences in LVD were found (Fig. 4b).

Discussion

Clinical findings in the present study were similar to those found in previous reports and did not show a significant pathological relationship with the vasculature in schwannoma.

Histopathologically, although both areas of Antoni A and B types were indicated in all cases, the Antoni A zone was more widespread than the Antoni B zone. The histopathological findings of Antoni A type is the most characteristic feature of schwannoma and is important to distinguish from other peripheral nervous tumors and soft tissue tumors (1-4). Because the Antoni B zone shows a diffuse proliferation of the tumor cells without nuclear palisading, it is difficult to distinguish Antoni B type schwannoma from neurofibroma and nerve sheath myxoma, myxofibroma, fibroma, or leiomyoma with myxoid change. Therefore, evidence of the Antoni A zone, even if the zone has a limited distribution, is important for making a definite diagnosis (2).

The histogenesis of the Antoni B zone could be explained by several theories, including degeneration and necrotic change of regressive disorders (11-16), over-expression of the myxoid matrix with progressive changes (17), and hemorrhage and edema by

disturbance of the circulation system (11-16). Our previous study examined the myxoid matrix of schwannoma and neurofibroma in which the histogenesis was associated with the expression of chondroitin-6 sulfate from the tumor cells and degeneration of the fibrous connective tissues (17).

In the present study, AB-positive myxoid matrix moderately appeared in the Antoni B zone, whereas unremarkable staining with PAS-AB was observed in the intercellular areas. These results indicate that the histogenesis of Antoni B zone is associated with not only myxoid degeneration and over-expression but also other factors, such as the circulation disturbance.

Immunohistochemically, the primary antibodies for CD34 and D2-40 were used in the present study. CD34 is a single-chain transmembrane protein of approximately 116 kDa and is specifically expressed in capillary endothelial cells (18). CD34 has been used in immunohistochemical studies of vasculature in neoplastic and other lesions (5, 6, 18). D2-40, the clone name of podoplanin, is a 38-kDa glycoprotein and is expressed in lymphatic endothelial cells but not in blood endothelial cells (19). D2-40 has been used in the studies of lymphangiogenesis in neoplastic lesions (7, 8, 19). Therefore, these antibodies are useful markers for blood and lymphatic vessels.

In the present study, CD34-positive blood vessels were found in every area of the Antoni A zone, border zone, Antoni B zone, and capsular tissues. Studies in developmental science have examined the biological and embryological interaction between vasculo- and neurogenesis (20, 21). In peripheral tissues, the congruence of the patterns of blood vessels and nerves is thought to reflect both the physiological dependency of nerves on oxygen and nutrients and the requirement of blood vessels to have appropriate vasoregulation (20). The patterning of blood vessels and nerves is associated with nerve-derived vascular endothelial growth factor. In addition, neural development and differentiation depend on blood vessels. For instance, in the adult central nervous system, clusters of neural stem cells proliferate in vascular niches that are enriched with endothelial-derived growth factors that stimulate neurogenesis (20, 21).

Eichmann et al. (20) suggested that axon guidance influenced vascular network formation with biological similarity and cooperation. Thus, the localization of CD34-positive blood vessels suggested that the blood vessels provided oxygen and nutrients for tumor growth. In another hypothesis, the proliferating tumor cells originating from Schwann cells might accelerate with angiogenesis.

D2-40-positive lymphatic vessels were predominantly distributed in the Antoni B zone and capsular tissue and were moderately observed in the Antoni A zone. The LVD showed a higher density in the Antoni B zone and capsular tissue. In tumor pathology, malignant tumor cells accelerate lymphangiogenesis and cause lymphatic metastasis; however, the lymphangiogenesis in benign tumors is not fully elucidated (8, 19). The lymphatic vessels adjacent to the peripheral nerves in the present study may be involved during Schwann cell tumorigenesis. Although the histological interaction of nerves and lymphatic vessels is not fully understood, Furukawa et al. (22) reported a topographic study of nerve-associated lymphatic vessels in the murine craniofacial region. This study suggested that the lymphatic system associated with the cranial nerves provided the pathway for transport of cerebrospinal and tissue fluids. In the present study, D2-40-positive lymphatic vessels were predominantly observed in the Antoni B zone and capsular tissue. These results suggest that edematous change from the lymphatic disturbance causes alienation of the tumor cell adhesion from the capsular tissue and the peripheral area of the tumor tissue, causing the formation of the Antoni B zone during tumor growth.

One case in the present study showed multicystic growth. Several histopathological studies of cystic schwannoma have been reported (11-16, 23, 24). The histogenesis is associated with the Antoni B zone, advanced degeneration, and the production of myxoid matrices, hemorrhagic necrosis with foamy cell accumulation, and edema. Other studies have reported true cyst or glandular formation in schwannoma (23, 24). These studies indicated that metaplas-

tic change in Schwann cell-like tumor cells might occur in tumor development. The present immunohistochemical results show no cytokeratin in any other component, including cyst-lining cells (data not shown), suggesting that epithelial metaplasia is not related to the formation of the multicystic spaces in the present cases or previous cases of pseudocystic formation (11-16). The present multicystic case also exhibited amorphous substances with AB-negative staining in the cystic spaces. In addition, positive reactivity for D2-40 was indicated in the cyst-lining cells. These results suggest that multicystic formation is associated not only with degeneration and over-expression of myxoid matrices but also with edematous change from circulation disturbance.

Edema is caused by conditions that interfere with the normal movement of blood, tissue fluid, and lymph or conditions that disturb the mechanism of fluid balance. Disruption of fluid balance can result from lymphatic obstruction, increased vascular permeability, increased capillary blood pressure, decreased plasma proteins, decreased hydrostatic pressure, increased colloid osmotic pressure, and sodium and water retention (25). The edematous change predominantly appeared in the Antoni B zone and the border zone as a result of these factors during tumor growth and development. Furthermore, edema is general pathologically divided into categories such as lymphedema, inflammatory edema, and angioneurotic edema as the result of localized edema and cardiac edema as the result of systemic edema (25). The edematous change in the schwannoma corresponded to lymphedema and/or angioneurotic edema, suggested by the dilation or hyperplasia of the CD34-positive blood vessels or D2-40-positive lymphatic vessels with a minimal level of inflammatory cell infiltration in the present results.

The results suggest that the localization of the blood and lymphatic vessels is closely related not only to degeneration and over-expression of the myxoid matrix but also to edematous change from circulation disturbance predominantly in the Antoni B zone during benign tumor growth and development.

Conclusion

The localization of the blood and lymphatic vessels in schwannoma using histopathological and immunohistochemical methodologies was investigated to elicit additional knowledge of the characteristics of oro-maxillofacial schwannoma in the present study and the following results were obtained.

1. The tumor parenchyma consisted of a proliferation of relatively long spindle cells with nuclear palisading (Antoni A type) and diffuse spreading with myxoid or edematous background (Antoni B type). In one case, the tumor exhibited multicystic growth.
2. Dilation and hyperplasia of the vessels were observed in the Antoni A and B zones, border zone, and capsular tissue.
3. In PAS-AB, the myxoid matrix in the Antoni B zone was stained blue.
4. Immunohistochemically, CD-34-positive blood vessels were found in all cases. The vessels were predominantly observed in the Antoni B zone and moderately observed in the Antoni A, the border of the Antoni A and B zones, and the capsular tissue. Four cases showed that D2-40-positive lymphatic vessels were mainly observed in the Antoni B zone and capsular tissue and moderately in the Antoni A. In the other four cases, D2-40-positive lymphatic vessels were only indicated in the capsular tissue. In addition, positive immunoreactivity for D2-40 was found in the cyst-lining cells of the multicystic case.
5. Microvessel density (MVD, numbers of blood vessels per unit area (0.15 mm^2)) was calculated for CD-34-positive blood vessels. MVD was 3.4 ± 2.1 in the Antoni A zone, 6.0 ± 1.7 in the border zone, 9.4 ± 3.2 in the Antoni B zone, and 2.7 ± 1.0 in the capsular tissue. Lymphatic vessel density (LVD, numbers of lymphatic vessels per unit area (0.15 mm^2)) was calculated for D2-40-positive vessels. LVD was 0.2 ± 0.5 in the Antoni A zone, 2.7 ± 3.5 in the Antoni B zone, and 2.4 ± 0.9 in the capsular tissue.

These results suggest that the localization of the blood and lymphatic vessels is closely associated

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 1. Histopathological findings

- The tumor consists of proliferating spindle cells with nuclear palisading (Antoni A type, AA). The tumor with loose connective tissue-like arrangement (Antoni B type, AB) is also observed. (Hematoxylin-eosin staining (HE); original magnification $\times 100$) (in-set, high power view of nuclear palisading in Antoni A zone; original magnification $\times 600$)
- Multicystic tumor (*, cystic space) (HE; original magnification $\times 100$)
- Vascular space is found in Antoni A zone. (HE; Original magnification $\times 400$)
- Vascular spaces with relatively thick wall are indicated in Antoni B zone. (HE; Original magnification $\times 400$)
- Vascular spaces are observed in border zone of Antoni A (AA) and Antoni B (AB). (HE; Original magnification $\times 400$)
- Findings of periodic acid-Schiff reaction-alcian blue pH2.5 staining. Antoni B zone (AB) is stained blue. Negative staining is observed in the vascular spaces. (*, cystic space) (original magnification $\times 100$)

Fig. 2. Immunohistochemical findings of S-100 β and CD34

- Positive immunoreactivity for S-100 β is observed in the tumor cells. (original magnification $\times 100$)
- CD34-positive vessels. (original magnification $\times 200$)
- CD34-positive vessels in Antoni A zone. (original magnification $\times 400$)
- CD34-positive vessels in border zone. (original magnification $\times 400$)
- CD34-positive vessels in Antoni B zone. (original magnification $\times 400$)
- CD34-positive vessels around cystic spaces (*, cystic space) (original magnification $\times 400$)

Fig. 3. Immunohistochemical findings of D2-40

- D2-40-positive vessels scattered in Antoni B zone and capsular tissue (AB, Antoni B zone; CT, capsular tissue) (original magnification $\times 100$)
- D2-40-positive vessels in Antoni B zone (original magnification $\times 400$)
- D2-40 positive cells appeared in intraluminal side of the cyst wall (*, cystic space) (original magnification $\times 400$)

Fig. 4. Microvessel density (MVD) and lymphatic vessel density (LVD) (number of positive vessels at high power field (unit area, 0.15 mm²))

- MVD
- LVD

with the histogenesis of the Antoni B zone in schwannoma, not only by the degeneration and over-expression of the myxoid matrix but also by the edematous change from circulation disturbance in the tumor tissues during benign tumor growth and development.

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References

- Weiss SW, Goldblum JR (Editors): Enzinger and Weiss's Soft Tissue Tumors, Fourth Edition, Mosby, St. Louis, 2001, p.1146-1173.
- Ushigome S, Machinami R (Editors): Atlas of Soft

- Tissue Tumors, Bunkodo, Tokyo, 1993, p.127-128. (*in Japanese*)
3. Shafer WG, Hine MK, Levy BM (Editors): A Textbook of Oral Pathology, Fourth Edition, WB Saunders, Philadelphia, 1983, p.206-210.
4. Williams PL, Bannister LH, Berry MM, Collins P, Dyson M, Dussek JE, Ferguson MWJ (Editors): Gray's Anatomy, The Anatomical Basis of Medicine and Surgery, 38th Edition, Churchill Livingstone, New York, 1995, p.398-399.
5. Desai RS, Mamatha GS, Khartri MJ, Shetty SJ: Immunohistochemical expression of CD34 for characterization and quantification of mucosal vasculature and its probable role in malignant transformation of atrophic epithelium in oral submucous fibrosis. *Oral Oncology*, 46: 553-558, 2010.
6. Scardina G-A, Ruggieri A, Messina P, Maresi E: Angiogenesis of oral lichen planus. A possible pathogenetic mechanism. *Med Oral Pathol Oral Cir Bucal*, 14: 558-562, 2009.
7. Sarkis SA, Abdulah BH, Majeed BAA, Talabani NG: Immunohistochemical expression of epidermal growth factor receptor (EGFR) in oral squamous cell carcinoma in relation to proliferation, apoptosis, angiogenesis, and lymphangiogenesis. *Head & Neck Oncology*, 2, 2010. (*Epub ahead of print*)
8. Margaritescu CM, Raica M, Pirici D, Simionescu C, Mogoanta L, Stinga AC, Stinga AS, Ribatti D: Podoplanin expression in tumor-free resection margins of oral squamous cell carcinoma. An immunohistochemical and fractal analysis study. *Histol Histopathol*, 25: 701-711, 2010.
9. Maghraby HK, Alsarha AI, Saad RS: Peritumoral lymphatic vessel density as a prognostic parameter in endometrial carcinoma. An immunohistochemical study. *Indian J Pathol Microbiol*, 53: 465-469, 2010.
10. Sharma S, Sharma MC, Sarkar C: Morphology of angiogenesis in human cancer. A conceptual overview, histoprostic perspective, and significance of neoangiogenesis. *Histopathology*, 46: 481-489, 2005.
11. Wallace CJ, Fong TC, Auer RN: Cystic intracranial schwannoma. *Can Assoc Radiol J*, 44: 453-459, 1993.
12. Pendl G, Ganz JC, Kitz K, Eustacchio S: Acoustic neurinomas with macrocysts treated with gamma knife radiosurgery. *Stereotact Funct Neurosurg*, 66: 103-111, 1996.
13. Chan JKC, Fok KO: Pseudoglandular schwannoma. *Histopathology*, 29: 481-483, 1996.
14. Miyawaki T, Nakamura A, Hayashi H, Kurihara K: Macrocystic schwannoma in the seventh cervical nerve. *Plast Reconstr Surg*, 104: 789-792, 1999.
15. Deng A, Petrali J, Jaffe D, Sina B, Gaspari A: Benign cutaneous pseudoglandular schwannoma. A case report. *Am J Dermatopathol*, 27: 432-435, 2005.
16. Ide F, Obara K, Mishima K, Saito I: Intraparotid pseudoglandular schwannoma. *J Oral Pathol Med*, 35: 379-381, 2006.
17. Ozawa K, Utsunomiya T: A histopathological, histochemical, and immunohistochemical study of oral neurofibroma and schwannoma. With special reference to mucoid matrix formation. *Nihon Univ J Oral Sci*, 26: 156-164, 2000.
18. Felschow DM, McVeigh ML, Hoehn GT, Civin CI, Fackler MJ: The adapter protein CrkL associates with CD34. *Blood*, 15: 3768-3775, 2001.
19. Wicki A, Christofori G: The potential role of podoplanin in tumour invasion. *Br J Cancer*, 96: 1-5, 2007.
20. Eichmann A, Noble FL, Autiero M, Carmeliet P: Guidance of vascular and neural network formation. *Curr Opin Neurobiol*, 15: 108-115, 2005.
21. Weinstein BM: Vessels and nerves. Marching to the same tune. *Cell*, 120: 299-302, 2005.
22. Furukawa M, Shimoda H, Kajiwarra T, Kato S, Yanagisawa S: Topographic study on nerve-associated lymphatic vessels in the murine craniofacial region by immunohistochemistry and electron microscopy. *Biomed Res*, 29: 289-296, 2008.
23. Ferry JA, Dickerson GR: Pseudoglandular schwannoma. *Am J Clin Pathol*, 89: 546-552, 1988.
24. Brooks JJ, Draffin RM: Benign glandular schwannoma. *Arch Pathol Lab Med*, 116: 192-195, 1992.
25. Anderson WAD (Editor): Pathology, Mosby, St. Louis, 1971, p.96-107.