膀胱マラコプラキーの1例

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MALAKOPLAKIA OF URINARY BLADDER

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Malakoplakia of the urinary bladder, first named by von Hanseemann in 1903, has become a well-defined gross pathologic entity. The disease is characterized by soft plaques which have given the lesion its name. We present here a case report of Malakoplakia of urinary bladder which was found in a 28-year-old woman with anamnesis of systemic lupus erythematoses.

I. Clinical findings:

K.S., 28-year-old woman. Family history: Parents died of apoplexia cerebri. Personal history: She was with appendectomy when 19 years old, was married at 26. She was first referred to us in April 1961 with erythema on the back of the hands as well as on both sides of the face in dark red butterfly shapes, systemic languor, a weak appetite, and a high fever (39°C). She was hospitalized for our dermatological treatment with diagnosis of "systemic lupus erythematoses". By means of steroid and antibiotic therapy, she made a favorable progress and was released from the hospital. She was hospitalized again on July 10, 1963 with a high fever of 39°C., shoulder pain, knee pain, headache, sore throat and spreading erythema on the face. She improved satisfactorily and was released on December 12 of the same year.

Present History:

She complained of "frequency, pain of urination" around January 10 this year (1964). She came to hospital for the consultation on January 13. Urinalysis at the first examination: Cloudy urine, Albumin test (++) , Sugar (-), Urobilinogen normal. Sediment: Red blood

cell (+), White blood cell (++) , epithel (+), E. Coli (++) .

Cystoscopic finding at that time:

Cystoscopic examination revealed general hyperamia and some bleeding points beneath the mucosa. Diagnosis was coligenic cystitis. With a medication of Furadantin (300 mg/day) for five days the patient made a favorable turn. Again the patient complained of cloudy urine, pain of urination, burning and frequency around February 10, and therefore sought consultation.

Urinalysis at that time:

Cloudy urine, Albumin test (+), Sugar (—), Sediment: White blood cell (++) , epithel (+), bacterium (—), Culture: E. Coli (++) . Only Kanamycin was effective in sensitivity test. Culture of tubercle bacillus negative. Examination of the blood disclosed 11.2 g per cent hemoglobin, 3,560,000 red blood cells and 5,300 white blood cells, with a differential count of 42% segmented neutrophils, 7% nonsegmented neutrophils, 1% eosinophils, 50% lymphocytes. The blood NPN was 34.0 mg/dl. Creatinine was 0.95 mg/dl. Serum total proteins was 9.2 g/dl. Specific gravity: 1.032 and included a serum Na of 134 m Eq/liter; cl: 105.5 m Eq/liter, K: 10.6 mg/dl. Serum protein fraction revealed the following: albumin 27.0%, alpha-1-globulin 11.3%, alpha-2-globulin 13.1%, beta globulin 14.4%, gamma globulin 34.1%. ASLO determination gives 120 units. CRP test was negative. The serologic test for syphilis was negative in the blood. IP showed bifid pelvis and ureter of right side. Examination of separated renal urine was not pathologic.

Cystoscopic finding at the second examination: (Fig. 1)

The whole of the mucous membrane of the bladder with the exception of the trigonum vesicae was strewn with canary yellow plaques, which varied in size from rounded or ovals. The central part was depressed. Around the edge of the plaque there was congested halo and there was no ulceration.

The mucous membrane apart from the plaques was healthy and the ureteric orifices were normal. It was decided that this finding was the case of Malakoplakia of the bladder, and so biopsy was applied to it.

II. Pathohistological findings (Fig. 2, 3, 4): "Granulomatous and exudative Cystitis."

Remarkable inflammations are recognized in the mucosa and the submucosa. In the former is found a granulomatous inflammation near the superficial layer and in the latter a degenerative, exudative inflammation. Granuloma consists of epithelioid histiocytes, giant cells, lymphocytes, plasma cells and fibroblasts on the increase. In the underneath area adjacent to these cellular nodules are found marked edema, swelling, fragmentation and partial eosinophilic homogenization of the collagen fibers in connective tissue. Within the giant cells can be found vacuoles. But Michaelis-Gutmann bodies are not discovered in the speci-

Fig. 1. Cystoscopic finding.

Fig. 2. The mucosa is denuded. The tunica propria shows rather diffuse plasmocytic infiltration and edema.

Fig. 3. Localized collection of neutrophils in a part of mucosa.

Fig. 4. Granulomatous lesion with multinucleated giant cell and epithelioid cells.

men. The mucosal epithelium on the surface of the granuloma are mostly come off. In a part have formed even ulcers together with infiltration of neutrophils. It seems that this case has every reason to be considered as one characteristic of mixture of two different kinds of inflammation, which perhaps will show a pattern cannot be placed in any other categories of disease. This definitely is not an inflammation caused by any heterogenecus substance. It is then rather to be suggested that this case has been caused by some certain allergen.

III. Comment: A. Pathological observation.

Malakoplakia, being derived from two Greek words meaning soft and plaque, connotes the formation of soft plaques on the mucous membrane of the hollow organ. The lesion may occur in the bladder, ureters and renal pelvis and may be recognized cystoscopically and autoptically. But the reported cases of the lesion are very rare. In 1902 Michaelis and Gutmann first reported the case and in 1903 von Hansemann named it "Malakoplakia." In 1918 Blum first made its cystoscopic examination and biopsy.

1. On Gross findings:

There is no consistent distribution of the lesions. They may be localized in one area or they may be scattered over the entire mucosa. The number of the lesions may range from a few to several hundred. The diameter ranges from 0.1 to 3 cm. Sometimes conglutination occurs among the lesions. They are circular, oval, or pseudomorphic, often having depressed centers like navels surrounded by a zone of hyperemia. They are gray-brown or canay yellow in color.

2. On histological findings:

The characteristic structure of this disease are large, mononucleated phagocytic cells, and Michaelis-Gutmann bodies which are thought to be deposits of calcium and iron. Phagocytic cells are large in size, and are circular, oval, or polyhedral. They are mononucleated. In view of their reticul production, their phagocytic nature, and their shapes originated from fibroblast, they seem to be macrophages that came from histiocytes. Soft plaques are an accumulation of histiocytes, plasma cells, and lymph cells, remarkably characterizing the main structure pattern of this disease. The most characteristic of the structure are Michaelis-Gutmann bodies which can be identified in most of the cases. They are circular or oval and 1—10 μ in size and are present within or among phagocytic cells, having affinity toward hematoxylin. In these bodies are proved the presences of calcium by von Kossa stain and of iron by Gomori stain, and Wells believes that bodies are not specific for malakoplakia, since he found them in three cases of banal cystitis. Wells holds an "infiltration" theory and Morison a "cell degeneration" theory. Loels proposed that these bodies could experimentally be produced by incubating blood, bouillon, urine, and colon bacilli, and Bunting emphasized that they resembled the inclusion seen in Boeck's sarcoid, corpora amylacea of the prostate. Ac-

according to Nation the characteristic of this disease is "mononuclear trophism." More recently in 1962 C.F. McKiel and others came out, by electron-microscopic examination, with a belief that the basic nature of Malakoplakia as a chronic inflammatory process located beneath the transitional epithelium of the bladder and that Michaelis-Gutmann bodies result from cystoplasmic granules. For other rare instances, Hankhol and Chinchianian reported a case of Malakoplakia of the testicle, and Hoffmann and Garrido reported a Malakoplakia fo the prostate. The etiology of this disease is unknown. Most of these who have seen this lesion believe it to be the result of an inflammatory process. However, some authors have suggested a variety of etiologies including neoplasm, tuberculosis, Boeck's sarcoid, pre-existing adrenal rest stimulated by *Escherichia coli*, fungus disease and virus infection. But the consensus today is that this disease is granuloma of unknown origin, and is selflimited.

B. Review of Literatures:

In 1956 Melicow presented the cases of the disease after Michaelis and Gutmann as well as the cases he treated himself, while here we have gathered up more recent cases reported after then, and also have introduced the case we had, and particularized the evidence of Michaelis-Gutmann bodies in it. Bleisch and Konikov identified four cases of Malakoplakia in 25,030 autopsies, which makes a 0.0016% incidence. There has been no case report of Malakoplakia vesicae in Japan but that of Dr. Yutaka Kobayashi in 1938. The following is a bibliography from the literatures of other countries:

Year	Pubilication	No. Cases	sex	Age	Discovered at	Michaelis-Gutman bodies
1902	L. Michaelis and C. Gutmann: Z. klin. Med, 47:208	2	♀	42	Autopsy	+
			♀	46	Autopsy	+
1903	von Hanseemann: Virchow Arch. Path. Anat. 173:302	2	♂	66	Autopsy	+
			♀	70	Autopsy	+
1904	K. Landsteiner and O. Stoerk: Beitr. z. path. Anat. u.z. allg. Path., 36:131	3	♀	67	Autopsy	+
			♀	40	Autopsy	+
			♂	Middle age	Autopsy	+
1905	E. Gierke: München Med. Wschr., 29:1388	2	♀	43	Autopsy	+
			♀	54	Autopsy	+
1905	K. Schmorl: München Med. Wschr., 29:1704	1	♀	96	Autopsy	+
1905	Guterbrock: Disseratied on Schmorl's article	1	♀	80	Autopsy	+
1906	K. Hart: Z. Krebsforschung 4:380	1	♂	41	Autopsy	+
1906	E. Frankel: München Med. Wschr., 53:242	2	♀	9 old	No sufficient account	
1906	R. Kimla: Virchow Arch. Path. Anat. 184:469	2	♂	23	Autopsy	+
			♂	37	Autopsy	+
1906	S. Minelli: Virchow Arch. Path. Anat. 184:157	1	♀	old	Autopsy	+

1906	A.M.Pappenheimer: Proc. N.Y. Path. Soc. N.S. 6:65	2	♀	64	Autopsy	+
			♀	53	Autopsy	—
1907	H. Wildbolz: Z. Urol., 1:323	1	♂	27	Autopsy	—
1907	W. Zangemeister: Z. Urol., 1:877	1	♀	43	Cystoscopy	obscure
1907	G. Berg: Deutsch. Med. Wschr., 35:1722	1	—	—	Biopsy	+
1909	Bethke: München Med. Wschr., 56:1619	1	♀	41	Autopsy	—
1909	H. Schmid.: Rev. Med. Suisse Rom. No. 11	3	♀	41	Autopsy	+
			♀	42	Autopsy	+
			♂	68	Autopsy	—
1910	W. Loele: Beit. zur Path. Anat., 48:206	1	♀	76	Autopsy	+
1910	Wegelin: Korresp-Bl. Schweiz. Arz. 40:234	1	♀	63	Autopsy	+
1911	Hedrén: Nord. Med. Ark., 44 : I	1	♀	45	Autopsy	+
1911	Panizzoni: G. ital. Mal. vener. 6:677	1	♀	25	Autopsy	—
1912	Loth: München Med. Wschr., 26:1463	1	♀	72	Autopsy	+
1912	Waldschmit: Z. Urol., 6:541	1	♀	78	Autopsy	+
1913	Schmidt: Frankfurt Z. Path., 14:493	1	♀	48	Autopsy	+
1913	E. Wetzel.: Virch. Arch. Path. Anat., 214:450	1	♂	69	Autopsy	—
1913	S. McDonald and W.T. Sewell: J. Path. Bact., 18:306	1	♀	24	Autopsy	+
1918	V. Blum: Wien. Med. Wschr 68:347	1	♀	40	Cystoscopy & Biopsy	+
1919	A. I. Folsom: J.A.M.A., 73:1112	2	♀	43	Cystoscopy & Biopsy	+
			♀	?	Cystoscopy- & Biopsy	—
1921	R. Ramacke: Z. Urol., 15:92	2	♀	51	Autopsy	+
			♂	63	Autopsy	+
1922	E. Osterich: Beitr. Path. Anat. 70:342	1	♂	51	Autopsy	+
1923	Thomson-Walker and J. Barrington, Proc. Roy. Soc. Med., 16: (Section of Urology) 32	1	♀	43	Cystoscopy & Operation	+
1924	A.C.Demel: Pathologica, 16:559	1	♀	29	Autopsy	obscure
1924	E. Opperman: Z. Urol., 18:64	1	♀	8	Autopsy	+
1926	P. Heilmann: Beitr. Path. Anat. 75:216	1	♀	73	Autopsy	+

1927	Z. Kairis-Athen. Virchow Arch. Path. Anat. 266:788	1	♀	15 months	Cystoscopy & Operation (Nephrectomy)	+(pelvis)
1927	W.E.C. Dickson, A.C.F. Gray and F. Kidd: Urol. Cutan. Rev., 31:611	1	♀	24	Cystoscopy	—
1929	F.H. Redewill: J.A.M.A., 92:532	1	♂	62	Cystoscopy & Biopsy	+
1934	A.E. Chisholm and G.R. Tudhope: Edinb. Med. J., 41:626	1	♀	61	Operation & Biopsy	—
1939	D.F. Rudvick and A.B. Ragins: J. Urol., 42:108	1	♀	53	Cystoscopy & Biopsy	+
1943	F.H.Redewell: J. Urol., 49:401	2	♀	40	Cystoscopy & Biopsy	+
			♂	62	Cystoscopy & Biopsy	+
1944	J.E. Morison: J. Path. Bact., 56:72	1	♀	6	Autopsy	+
1946	D.S. Cristol and A.C. Broders: J. Urol., 55:260	2	♀	52	Cystoscopy & Biopsy	+
			♀	35		
1950	C.E. Boonstra and P.L. Bates: U.S. Armed Forces Med. J. 1:1029	1	♀	25	Cystoscopy & Biopsy	+
1951	E. Hagemann Z. Urol., 44:9	1	♀	31	Cystoscopy & Biopsy	+
1951	A.J. French and J.T. Mason: J. Urol., 66:229	1	♀	41	Cystoscopy & Biopsy	+
1952	V.R. Bleich and N.F. Konikov: Arch. Path., 54:388	4	♀	41	Autopsy	+
			♀	44	Autopsy	+
			♀	74	Autopsy	+
			♀	46	Autopsy	+
1953	W.H. Bennett: J. Urol., 70:84	3	♀	40	Cystoscopy	+
			♀	39	Autopsy	—
1956	E.F. Nation: J. Urol., 76. 576	1	♀	74	Cystoscopy & Biopsy	—
1957	M.M. Melicow: J. Urol., 78:33	1	♀	64	Cystoscopy & Biopsy (Cystectomy)	+
1958	E.V.Z. Scott and W.F. Scott: J. Urol., 79:52	1	♀	64	Autopsy	+
1961	W.R. Curtis, J.D. Bozzell and C.L. Green: J. Urol., 86:78	1	♀	34	Cystoscopy & Biopsy	+
1962	C.F. McKiel, R. Eisenstein and J.H. McDonald J. Urol., 88:236	1	♀	33	Cystoscopy & Biopsy	+
1962	A. Angelov: Z. Urol., 52:371	1	♀	58	Cystoscopy & Biopsy	+
1964	H. Sasaki and M. Hokano	1	♀	28	Cystoscopy & Biopsy	—

Summary of Publications:

Total cases 71 Sex: ♂ 11, ♀ 58, unknown 2.

Age 0— 9..... 4

10—19.....	0
20—29.....	8
30—39.....	6
40—49.....	20
50—59.....	7
60—69.....	12
70—79.....	7
80	2
Unknown	5
Diagnostic Confirmation:	
Autopsy	44
Cystoscopy	2
Cystoscopy & Biopsy	18
Biopsy	1
Cystoscopy & Operation	3
Operation & Biopsy	1
Unknown	2
Michaelis-Gutmann bodies:	
Positive	55
Negative	12
Unknown	4

Conclusions:

An additional case of Malakoplakia in a 28-year-old woman has been reported. The disease is more common in females and its greatest incidence is in the fourties. Malakoplakia is a unique non-specific inflammatory response of the urinary tract to coliform infection. It is characterized by yellow or brown submucosal plaques composed largely of histiocytes and lymphocytes and often containing Michaelis-Gutmann bodies.

We wish to express appreciation to Prof. S. Suzuki, urologist, and Prof. Y. Otaka, pathologist, for their contribution in the study of this case.

膀胱 Malakoplakia は1903年 von Hanseman によって始めて命名され、以来明確に一つの疾患として規定された病変である。この疾患は病変の呈する軟かい結節斑形成に特色がある。吾々は systemic lupus erythematoses の既往歴を有する28才家婦に膀胱 Malakoplakia と考えられる症例を経験したので報告する。

I. 臨床的事項

K.S. 28才の家婦，家族歴，両親とも脳溢血で死亡。既往歴，19才の時に虫垂切除手術を受け，26才で結婚，

昭和36年4月頃より両手背に紅斑が出現。顔面，両頬部に蝶形暗赤色の紅斑が発生し，全身の倦怠感，食欲不振，発熱（39℃）を訴え，“systemic lupus erythematoses”の診断で当病院皮膚科に入院，ステロイド剤及び抗生物質療法により軽快退院した。昭和38年7月10日頃より発熱39℃，肩の痛み，膝の痛み，咽頭痛と共に顔面にびまん性の紅斑が発生して再入院し同年12月12日，軽快退院した。
現病歴

昭和39年1月20日頃より、尿意頻数、排尿痛を訴え、1月13日当科来院、初診時尿所見、外見濁濁、蛋白反応(++)、糖反応(-)、Urobilinogen(-)、沈渣：白血球(++)、赤血球(+),上皮(+),大腸菌(++)。

初診時の膀胱鏡所見

膀胱粘膜は全体的に充血と処々に粘膜下出血を認め、大腸菌性膀胱炎と診断し、Furadantin(1日300mg)、を5日間投与、軽快した。越えて2月10日頃より濁濁尿、排尿痛、尿意頻数を訴え再来院した。

再来院時尿所見

外見濁濁、蛋白反応(++)、糖(-)、沈渣：白血球(++)、上皮(+),細菌(-),尿培養 大腸菌陽性、感受性検査は Kanamycin のみ有効。

結核菌の培養は陰性。

血液検査成績：Hb 11.2 g/dl, 赤血球 356万, 白血球 5800でその分核は分葉好中球42%, 桿状7%, 好酸球1%, 淋巴球50%であった。NPN 34.0mg/dl, クレアチニン0.95mg/dl, 血清総蛋白 9.2 g/dl, 比重 1.032, Na: 134 mEq/L, Cl: 105.5mEq/L, K: 10.6mg/dl, 電気泳動像はアルブミン27.0%, α_1 11.3%, α_2 13.1%, β 14.4%, γ 34.1%, であった。ASLO は12単位で CRP は陰性であり、血清梅毒反応は陰性であった。排泄性腎盂撮影像では左の重複尿管と判明、分離尿所見は両側とも病的所見はなかった。

再診時膀胱鏡所見(附図1)

膀胱三角部を除いた粘膜に円形、楕円形のカナリヤ黄色を呈した結節斑を認めた。その中心部は陥凹し境界には充血があるが、潰瘍ではなかった。結節斑から離れた粘膜は健常で両側尿管口は正常であった。上述の所見から膀胱の Malakoplakia ではないかと診断し生検を施行した。

II. 生検組織診断“肉芽腫及び滲出性膀胱炎”(附図2, 3, 4)

粘膜固有層と粘膜下層に顕著な炎症を認め、前者では比較的表層に近い部に肉芽腫性炎症を、後者では変質性一滲出性をみる。肉芽腫は類上皮性の組織球、異物型巨細胞、リンパ球形質細胞及び線維芽細胞の増殖等によりなっている。この細胞性結節に接する深部には結合組織における強い水腫、線維の膨化、断裂、部分的な好酸球性均質化等の所見が認められる。巨細胞には空胞を認めるが、標本上では Michaelis-Gutmann 小体は認められない。肉芽腫形成部の表層にある粘膜上皮は剥離を示す所

が多く、一部に好中球浸潤を伴って、潰瘍形成の個所も認められる。これら両型式の炎症の混在とする特徴のある病変で、他のいずれの疾患にもあてはめられない組織像を示すものと云える。また単なる異物炎性の形式でもなく、何等かのアレルゲンによるアレルギー性炎症とみるのが至当と考えられる。

III. 考 按

A. 病理学的考察

Malakoplakia とはギリシャ語で軟かい斑の意味で、膀胱、尿管、腎盂に発生し、膀胱鏡、剖検によつて発見されるが、現在迄の報告例は極めて少ない。1902年 Michaelis 及び Gutmann が最初に発見し、翌1903年 von Hansemann は“Malakoplakia”と命名し、1918年 Blum は最初に膀胱鏡検査と生検を施行した。

1. 肉眼的所見について

好発部位は特にあげられず、結節斑は一部に限局することもあり、全粘膜に散在していることもある。その数はごく僅かの症例から数百に及ぶこともありうる。大きさは0.1~0.3cmで時に癒合することもある。形は円形、楕円形、又は不正形で、しばしば中心は陥凹し臍状で境界は鮮明で充血を伴う。色調は灰色、褐色、或は鮮黄色である。

2. 組織学的所見について

本症の組織所見の特徴は大きい単核性の喰細胞、及びカルシウムと鉄を含む Michaelis-Gutmann 小体である。喰細胞の形は大きく、円形、卵円形、多面体を呈し単核である。

この細胞は細網生成能、喰細胞的な性質を有し形態的には線維芽細胞からの移行という点からみて、細織球に由来する Macrophage とみなされる。結節斑は組織球、プラズマ細胞、リンパ球の集積で、本症の組織像の顕著な部分を形成している。

最も特徴とされるもの Michaelis-Gutmann 小体で、大多数の報告例に本小体が証明され円形、楕円形であり大きさは1~10uで、喰細胞中、或はその間に存在し、Haematoxylin に対し親和性があり、von Kossa 染色によりカルシウム、Gomori 染色により鉄が証明される。また Wells は非特異性膀胱炎の3例から本小体を発見し、本小体は必ずしもマラコプラキア特有の小体とは限らないと述べている。本小体については Wells は感染尿の浸潤説、Morison は細胞の変性説を唱えている。Loele は本小体は血液、肉汁、尿、大腸菌の封入によつて実験的に形成できるとし、Buntung は Boeck の肉

腫，前立腺腺粉様小体に類似していると説明している。
Nation は本症組織の特色は “Mononuclear trophism”
としている。最近1962年 C.F. McKiel 等は本症の電顕
像から，Malakoplakia の本態は膀胱の移行上皮下に位
置する慢性炎症性機能で，Michaelis-Gutmann 小体は
原形質顆粒から転ずると説いている。稀有な症例として
Hankhol 及び Chinchianian は睪丸の，Hoffmann 及び
Garride は前立腺の本症を報告している。従つて本症は
膀胱のみに限定した疾患ではない。

本症の原因については未だ不明である。腫瘍説，結核
説，Boeck の肉腫説，大腸菌により刺戟された膀胱内
副腎組織遺残説，糸状菌説，ウイルス説が提唱されてい
るが，現在では本症は原因不明の肉芽腫とみなすが諸家
の一致した意見のようである。

B. 文献的考察

1956年 Melicow は Michaelis 及び Gutmann 以来の症
例に自験例を加えて報告しているが，吾々は Melicow 以
降の症例及び個々の症例における Michaelis-Gutmann
小体の存在について調査した。Bleich 及び Konikov は
剖検の25,030例中で僅かに4例即ち 0.016%の頻度とし
ている。本邦では本症については1938年，小林豊博士の
報告を見るに過ぎないが，その詳細は不明である。

報告例のまとめ：（個々の症例に就いては英文参照の
こと）。

総数：71例	
性別：男11例，女58例，不明2例	
年令別：	
0～9才	4例
10～19才	0例
20～29才	8例

30～39才	6例
40～49才	20例
50～59才	7例
60～69才	12例
70～79才	7例
80才以上	2例
不明	5例

診断の根拠：

剖検	44例
膀胱鏡	2例
膀胱鏡＋生検	18例
生検	1例
膀胱鏡＋手術	3例
手術＋生検	1例
不明	2例

Michaelis-Gutmann 小体の証明数：

陽性	55例
陰性	12例
不明	4例

結 語：

28才家婦の膀胱 Malakoplakia の症例を追加報告す
る。本症は女性に多く，年令的には40才代に頻度が高
い。Malakoplakia はユニークな非特異性炎症で，本症
の特徴は鮮黄色又は褐色の色調を呈する結節斑である。
吾々は Melicow 以降の症例と主として個々の症例に於
ける Michaelis-Gutmann 小体の存在の有無について文
献的考察を試みた。

稿を終るにあたり，本発表について御指導，御校閲を
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References

(We have not brought up case reports here in these references.)

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