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SVC syndrome in King Chulalongkorn Memorial Hospital

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Suwanrusme H, Sriuranpong V, Apinonkul K, Voravud N. SVC syndrome in King Chulalongkorn Memorial Hospital. Chula Med J 1998 Dec; 42(12): 1079-90

- Objective** : *To determine clinical features, diagnostic and therapeutic outcome of SVCs in Chulalongkorn Hospital*
- Setting** : *Medical Oncology Unit, Department of Internal Medicine, Faculty of Medicine Chulalongkorn University.*
- Design** : *Descriptive clinical study*
- Patients/Material** : *Clinical records of 28 SVCs cases treated at the Medical Oncology Unit from 1992-1995.*
- Methods** : *A review of all clinical records of 28 SVCs cases was carried out to determine the patient characteristics, presenting symptoms and signs, diagnostic and treatment methods*
- Results** : *There were 24 males and 4 females SVCs patients. Median age was 52.0 years (16-80). Seven patients (25%) were less than 35 years old. SVCs was the presenting symptom of underlying malignancy in 23 cases (82.11%). Typical symptoms included facial swelling 96.4%, arm swelling 78.5%, dyspnea 78.5%, and cough 64.3%. Less common symptoms were chest pain 17.9%, head pullness 39.3%, hoarseness 25.0%, dysphagia 7.1%, hemophysis 3.6% and syncope 3.6%. The frequent clinical findings were facial swelling 69.4%, increased collateral veins of the anterior chest wall 87.3%, venous distention of neck 82.1% and swelling of arms 78.5%. Common chest*

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roentgenograph findings were right hilar mass (57.1%), mediastinal widening (50.0%), and plural effusion (42.8%). CAT scan of chest was performed in 19 patients which all yielded positive findings. Bronchoscope examination yielded positive in 2 of 7 cases. Fine needle aspiration biopsy had positive result in 10 of 13 cases. The most common etiology was lung cancer. In the younger aged group (< 35 years), treatable malignancies were the important causes, such as germ cell tumor (4/7) and lymphoma (2/7). 8 of 9 patients responded to concurrent chemoradiation. 6 of 8 responded to chemotherapy alone. And only 3 of 9 responded to radiation treatment alone. According to histology, 7 of 12 non-small cell lung cancer, 5 of 6 small cell lung cancer, and 3 of 6 germ cell tumor responded to treatment. The overall response rate was 64.3%. The overall median survival time calculated by Kaplan-Meier's method was 10.9 weeks.

Conclusion : *The majority of SVCs patients in this study were non-small cell lung cancer patients. Younger patients had more chemosensitive malignancies such as germ cell tumor and lymphoma. Establishment of the extent of disease in the chest by imaging technich and a pathological diagnosis were crucial prior to a ppropriate therapy with either radiation or chemotherapy or both. FNA was an important diagnostic procedure with a high positive yield. Response to treatment depended on the underlying malignancies.*

Key word : *Superior vena cava syndrome.*

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หฤกษ์ สุวรรณรัศมี, วิโรจน์ ศรีอุฬารพงศ์, กาญจนา อภินนทกุล, นรินทร์ วรวุฒิ. ภาวะอุดกั้นหลอดเลือดดำ ซูพีเรียร์ วินา คาวา ในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2541 ๕.ค; 42(12): 1079-90

- วัตถุประสงค์** : เพื่อศึกษาลักษณะทางคลินิก การวินิจฉัย และผลการรักษาภาวะอุดกั้นหลอดเลือดดำ ซูพีเรียร์ วินา คาวา ในโรงพยาบาลจุฬาลงกรณ์
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- รูปแบบการศึกษา** : การศึกษาเชิงบรรยาย
- ผู้ป่วยที่ทำการศึกษา** : ข้อมูลจากเวชระเบียนผู้ป่วย จำนวน 28 ราย ที่มีภาวะอุดกั้นหลอดเลือดดำ ซูพีเรียร์ วินา คาวา ซึ่งได้รับการรักษาในหน่วยมะเร็งวิทยาตั้งแต่ พ.ศ. 2535 - 2538
- วิธีการศึกษา** : โดยรวบรวมและวิเคราะห์ข้อมูลทางคลินิกของผู้ป่วยเพื่อศึกษาลักษณะผู้ป่วย อาการ และอาการแสดง การวินิจฉัย และการรักษา
- ผลการศึกษา** : ผู้ป่วยชาย 24 ราย หญิง 4 ราย ซึ่งมีภาวะอุดกั้นหลอดเลือดดำ ซูพีเรียร์ วินา คาวา อายุเฉลี่ย 52 ปี (16 - 80) มี 7 ราย อายุน้อยกว่า 35 ปี ภาวะนี้เป็นอาการนำของโรคมะเร็งในผู้ป่วย 23 ราย (82.11%) อาการบ่งชี้สำคัญประกอบด้วย หน้าบวม 96.9%, แขนบวม 78.5%, หายใจลำบาก 78.5% และ ไอ 64.3% อาการที่พบบ่อย เช่น เจ็บหน้าอก 17.9%, หนักศีรษะ 39.3%, เสียเหงื่อ 25.0%, กลืนลำบาก 7.1%, ไอเป็นเลือด 3.6% และหมดสติ 3.6% อาการแสดงที่ตรวจพบได้บ่อย เช่น หน้าบวม 69.4% การขยายตัวของหลอดเลือดดำบริเวณผนังทรวงอกส่วนหน้า 87.3% การคั่งของหลอดเลือดดำบริเวณคอ 82.1% และแขนบวม 78.5% ลักษณะภาพรังสีทรวงอกที่พบบ่อยคือ ก้อนบริเวณซั้วปอดขวา 57.1% เมดิแอสติเน็ทกว้าง 50% และน้ำในช่องปอด 42.8% การทำเอ็กซเรย์คอมพิวเตอร์ของทรวงอกในผู้ป่วย 19 ราย ทุกราย แสดงให้เห็นพยาธิสภาพ การส่องกล้องตรวจทางหลอดลมได้ผลการวินิจฉัย 2 รายจาก 7 ราย การเจาะดูดชิ้นเนื้อด้วยเข็มได้ผลการวินิจฉัย 10 จาก 13 ราย สาเหตุที่พบบ่อยที่สุดได้แก่มะเร็งปอด ในผู้ป่วยอายุต่ำกว่า 35 ปี จะพบมะเร็งที่ตอบสนองต่อการรักษา เช่นเนื้องอกจิร์มเซลล์ (4/7) และมะเร็งของเนื้อเยื่อต่อมน้ำเหลือง (2/7) ผู้ป่วย 8 ใน 9 ราย ตอบสนองต่อการรักษาด้วยเคมีบำบัดร่วมกับรังสีรักษา 4 ใน 8 ราย ตอบสนองต่อเคมีบำบัดอย่างเดียว มีผู้ป่วยเพียง 3 ใน 9 ราย ที่ตอบสนองต่อรังสีรักษาเพียงอย่างเดียว

เมื่อพิจารณาจากลักษณะทางเนื้อเยื่อมะเร็งปอดชนิดไม่ใช้เซลล์ขนาดเล็ก 7 ใน 12 ราย ชนิดเซลล์ขนาดเล็ก 5 ใน 6 ราย และเนื้องอก เจริ้มเซลล์ 3 ใน 6 ราย ตอบสนองต่อการรักษา อัตราการตอบสนองต่อการรักษา โดยรวม 64.3% ระยะเวลารอดชีวิต (มีรยฐาน) คำนวณโดยวิธีคาแปลนเมเยอร์ คือ 10.9 สัปดาห์

สรุป

- : สาเหตุสำคัญของภาวะอุดกั้นหลอดเลือดดำ ซูพีเรียร์ วินา คาวา ในการศึกษา นี้ คือมะเร็งปอดชนิดไม่ใช้เซลล์ขนาดเล็ก ผู้ป่วยอายุน้อย จะพบมะเร็งที่ตอบสนองดีต่อเคมีบำบัดมากกว่า เช่น เนื้องอกเจริญเซลล์และมะเร็งเนื้อเยื่อ น้ำเหลือง การวินิจฉัยการลุกลามของพยาธิสภาพในทรวงอก โดยเทคนิคทางรังสีวิทยา และการตรวจชิ้นเนื้อทางพยาธิวิทยา มีความสำคัญเพื่อนำไปสู่การรักษาที่เหมาะสมไม่ว่าโดยรังสีรักษาและ/หรือ เคมีบำบัด การวินิจฉัยในการใช้เข็มเจาะกระดูกเนื้อเยื่อเป็นวิธีที่ได้ประโยชน์สูง การตอบสนองต่อการรักษาขึ้นอยู่กับโรคมะเร็งที่เป็นสาเหตุเป็นสำคัญ

The superior venacava syndrome (SVCs) is characterized by edema of the head, neck, arms, and upper trunk with dilated collateral veins and is often accompanied by cyanosis, dyspnea, headache and altered mental status. It causes significant morbidity and mortality from cerebral edema, reduced cardiac output, and upper airway obstruction which requires rapid diagnosis and treatment by the physician.⁽¹⁾ Over the years, the picture of SVCs has changed since the original etiologic classification presented by McIntire and Sykes in 1949⁽²⁾ in which they concluded that one third of the cases were due to primary intrathoracic tumors, one-third to aortic aneurysms, and the remaining third to chronic mediastinitis and a number of less frequent conditions. Many later review have shown a steady decline in the number due to aortic aneurysms and alarming increases in the number due to malignancy, both primary lung cancer and mediastinal malignancy. Because SVCs is generally regarded as an oncologic emergency, therapy is often initiated before a diagnosis is firmly established. More over, invasive diagnostic procedures are considered hazardous by many, mainly because of excessive bleeding and respiratory complications.⁽³⁻⁶⁾ There is controversy about the proper way of management, such as diagnostic procedures in obtaining histology and choices of treatment. We have reviewed the past 5 years experience with SVCs in Chulalongkorn Hospital to determine clinical features and diagnosis and therapeutic outcome.

Methods

A review of all clinical records of 28 SVCs cases in responsibility of Medical Oncology unit, Chulalongkorn Hospital was carried out to determine the patient characteristics, presenting symptoms and

sign, chest x-ray appearance, method of diagnosis, causes of SVCs, and treatment and follow up between the years 1992 to 1995.

Result

Twenty-eight cases of SVCs were diagnosed from that period. There were 24 males (85.7%) and 4 females (14.3%), with an average age of 49.7 years (range from 16 to 80 years).

*Clinical presentation (Table 1-2)

In 23 of 28 patients (82.1%), the SVCs was the presenting symptom of their disease. The most common presenting symptoms consisted of facial swelling in 27 (96.4%), arm swelling in 22 (78.5%), followed by respiratory complaints, such as dyspnea in 22 (78.5%) and cough in 18 (64.3%). Few patients had complaints of head fullness (11, 39.3%), hoarseness (7, 25%) or chest pain (5, 11.9%). Other less frequent-symptoms were dysphasia, hemoptysis and syncope.

Physical findings are summarized in table 2 and were generally associated with obstruction of the SVC: were facial edema in 27 patients (96.4%), increase collateral veins of anterior chest wall in 25 (89.3%), dilated neck vein in 23 (82.1%), and edema of the arms in 22 (78.5%). Airway obstruction and cyanosis were uncommon in our experience (14.3% and 3.6%).

Table 1. Age and sex.

Age	N	%
< 20	2	7.14
20-39	6	21.42
40-59	12	42.84
≥60	8	28.5

Mean age = 49.71 years Median = 52 years (16-80)

Table 2. Presenting symptoms.

	Chula, 1996		Yellin A, 1990	
	N	%	N	%
Facial swelling	27	96.4	54	85.7
Arm swelling	22	78.5	0	31.7
Dyspnea	22	78.5	19	30.2
Cough	18	64.3	13	20.6
Head fullness	11	39.3	-	-
Hoarseness	7	25.0	1	1.6
Chest pain	5	17.9	4	6.3
Dysphagia	2	7.1	4	6.3
Hemoptysis	1	3.6	5	7.9
Syncope	1	3.6	-	-

The most common chest x-ray abnormality (Table 3) were right hilar masses in 16 (57.1%) and superior mediastinal widening in 14 (50%). Other abnormalities included plural effusion, anterior mediastinal mass, bilateral diffuse infiltration and cardiomegaly.

No normal chest film was found in our patients.

The duration of symptoms before diagnosis of SVCs was 3.5 weeks in average. Most of the patients were diagnosed within 1 month since onset of symptoms.

Table 3. Clinical presentations.

	N	%
Facial edema	27	96.4
Increased collateral veins of the anterior chest wall	25	89.3
Venous distention of neck	23	82.1
Edema of arms	22	78.5
Plethora of face	8	28.6
Stridor	4	14.3
Cyanosis	1	3.6

***Underlying conditions and diagnosis procedures.**

Causes of superior vena cava obstruction are summarized in Table 4. For the 27 patients who obtained tissue diagnosis all of the histopathologies were malignant. For the other case, there was no tissue diagnosis. No benign histology was detected in our series. Bronchogenic carcinoma accounted for more than half of the cases (19, 67.8%). The second common cause of the SVCs was primary mediastinal tumor (6, 21.4%) and non-seminomatous germ cell tumor was responsible for the majority of this group (4, 14.3%). Lymphoma was found in two cases (7.1%). In patients younger than 35 either, the course of SVCs was primary mediastinal tumor, germ cell tumor or

Table 4. Chest film N = 28.

	N	%
Rt hilar mass	16	57.1
Sup mediastinum widening	14	50.0
Plural effusion	12	42.8
Ant mediastinal mass	9	32.1
Bilateral diffuse infiltration	1	3.6
Cardiomegaly	1	3.6
Normal	0	0

C-T Chest 19 cases (67.8%) doiaagnostic 19

lymphoma. In contrast older than 35, the major causes were primary lung cancer. (Table 5)

Table 5. Type of malignancy.

Malignancy	Suwanrusme H. 1996		Yellin A. 1990	
	N	%	N	%
*1 ^o Lung Cancer	19	67.8	30	47.6
- SCLC	6	21.4	4	-
- Squamous	4	14.3	6	-
- Adeno carcinoma	7	25.0	6	-
- Large cell	1	3.6	2	-
- Mixed SCLC + NSCLC 1	3.6	0	-	-
*1 ^o Mediastinum tumor	6	21.4	4	6.3
- Germ cell (seminoma)	1	3.6	1	-
- Germ cell (non seminoma)	4	14.3	-	-
- Thymoma	1	3.6	2	-
- Esophageal carcinoma	-	-	1	1
*Lymphoma	2	7.1	13	20.6

Table 6. Age classification by type of malignancy.

	Age	
	0-35 yr	>35 yr
NSCLC	-	12
SCLC	-	7
Germ cell tumor	4	1
Lymphoma	2	-
Others	1	-
Unknown	-	1

For diagnosis of SVC, chest computerized tomography were performed in 19 (67.8%) which all yielded positive findings. The most frequent invasive procedure that was done in our series appeared to be fine needle aspiration biopsy which have positive result in 10 of 13 cases. Bronchoscopy was performed less frequent and had surprisingly low positive yield (2 of 7). Lymph node biopsy had positive result in 6 of 7 cases. Various other less common procedures were also helpful in establishing the diagnosis, thoracentesis (2), plural biopsy (2), mediastinoscopy (2), and thoracotomy (1). (Table 7)

Table 7. Diagnostic procedures.

	Yellin A. 1990	
	N	Diagnostic
FNA	1	1
Bronchoscopy	13	8
Lymph node biopsy	7	5
BM biopsy + aspiration	-	-
Throacentesis	3	2
Plural biopsy	-	-
Mediastinoscope	15	14
Thoracotomy	1	1

***Treatment and outcome**

Treatment is summarized in Table 8 specific treatments aiming to alleviate the symptoms of SVC consisted of radiation therapy alone (9, 32.1%) chemotherapy alone (8, 28.7%), or combinations of chemotherapy and radiation therapy (9, 32.1%). Treatment with steroids (17, 60.7%), diuretics (6, 21.4%) and fluid restriction (7, 25.0%) were also used as adjunctive therapies. The type of specific treatment depended on the diagnosis. Lymphomas were treated with a curative intention. Patients with bronchogenic carcinomas, where the goal was to alleviate symptoms, were offered radiotherapy, with or without chemotherapy. The combination of chemotherapeutic agents or the amount of radiation were tailored according to the individual tissue diagnosis. The overall response rate was 64.3% (18 cases).

Table 8. Treatment.

Treatment	N	%
Steroid	17	60.7
Diuretics	6	21.4
Restrict fluid	7	25.0
Chemotherapy only	8	28.7
Concomitant chemoradiation	9	32.1
Radiotherapy only	9	32.1

For the responders, the time to subjective relief was 6.8 days in average, and for objective response, the average time to response was 12 days. According to histology, results there were 7 responders of 12 non-small cell lung cancers, 5 responders of 6 small cell lung cancers, and 3 responders of 5 germ cell tumors. When stratified by treatment modality, 8 of 9

patients responded to combined chemotherapy and radiation, 6 of 8 patients responded to chemotherapy alone, and in the radiation therapy alone there were only 3 responders out of 9 patients. The outcome of SVCs cases is also shown in Table 9. Of the 28 patients, 14 died (50%), and of these, 9 died from their underlying malignancy, 5 died from other causes, including 1 death

from treatment complication, febrile neutropenia. No patient died from SVCs. Six (21.4%) were alive at the end of reference period and 8 were lost to follow-up. The median survival time calculated by Kaplan-Meier's method for non-small cell lung cancer was 8.0 weeks, and for germ cell tumor was 20.29 weeks. The overall median survival time was 10.86 weeks. (Table 10)

Table 9. Outcome of different malignancies.

Etiology	N	Alive		Dead		Loss F/U	Rresponse	Non-response
		N		(W)				
			Median survival		Rage			
1. Lung Cancer	6	1	4	10.86	1.43-42.43	1	5	1
- SCLC	12	3	7	8	0.14-39.14	2	7	5
- NSCLC	1	1	-	-	11.71-31.14	-	1	-
2. Lymphoma	-	2	-	11.71	-	2	2	-
3. Germ cell	-	-	-	-	11.71-31.14	-	-	-
- NSGTC	4	1	1	20.29	-	2	3	1
- Seminoma	1	-	1	-	0.29-93.00	-	-	1
4. Thymoma	1	-	1	20.86	-	-	-	1
5. Undiagnose	1	-	-	-	-	1	-	1

Table 10. Treatment outcome.

N	Treatment	R	NR	Alive	Dead	Loss F/U	N
9	Chemo + XRT	8	1	2	6*	1	9
9	XRT only	3	6	2	4**	3	9
8	Chemotherapy	6	2	2	4***	2	8
2	Non XRT or Chemo	1	1	-	-	2	2

*3 died from other causes (in response group)

**1 died from other causes (in non response group)

***4 died from treatment complication (in response group)

Discussion

The superior venacava syndrome, first described by William Hunter in 1757 as a complication of a syphilitic aortitis,⁽⁷⁾ may result from various mediastinal conditions. In the past the etiologies consisted of a great number of benign conditions, such as aortic aneurysms, tuberculosis, and chronic mediastinitis.^(2, 8-10) Because of the declining incidence of benign conditions causing SVCs, as well as the increasing incidence of malignancies, the trend now has already shifted toward malignant conditions that constitute 85-90% of all cases.⁽¹¹⁻¹³⁾ The remaining benign conditions become a thrombosis related to intravenous catheter use rather than aneurysms or granuloma that once were the causes.⁽¹⁴⁾

The most common malignant tumor causing SVCs in our series was, same as the finding in many articles, bronchogenic carcinoma.⁽¹¹⁻¹⁴⁾

The common location of lung malignancy found in previous reports⁽¹¹⁾ and in this series was in the right lung which has a closer anatomical relationship to the superior vena cava.

About histological subtypes, small-cell lung cancers more often implicated. The average age at diagnosis of SVCs was 49.7 years, close to that for lung cancer. Using age 35 as a cut off point, no cases of lung cancer were found under that age. In the younger age group (<35), the etiologies were treatable malignancies, such as germ cell tumor and lymphoma. For unknown reasons. There was a prominent number of germ cell tumor (17.9%) in our series in comparable to others.^(12, 14, 15) However, we can conclude that we have to obtain an accurate diagnosis especially in the younger age group because their causes are usually malignancies that can be successfully treated in curable aim.

The clinical diagnosis of SVCs can easily be made at bedside. Almost all of SVCs patients have symptoms from venous obstruction, with or without respiratory complaints. Emergency symptoms such as hemoptysis or syncope can be found but they are very rare. Cerebral edema that cause severe changes in mental status and other serious neurological manifestations called "wet brain syndrome"⁽⁸⁾ was also never found in our series. The characteristic physical finding obviously seen is facial and upper trunk edema, distension of neck veins and collateral veins of the anterior chest wall. Stridor and cyanosis indicating airway obstructions were found in only few patients. From these findings, it seems that SVCs does not frequently cause true emergency conditions that leads to rapid deterioration of the clinical course. Our conclusion is confirmed by the outcome of our patients in which there were no deaths directly caused by the SVCs. The similar result that was reported by Schraufagle, et al⁽¹²⁾ in 1971 raised a question whether immediate radiotherapy was crucial for all SVCs cases or should tissue diagnosis be obtained in most cases before the beginning of treatment. They also commented that prior radiotherapy not only made subsequent surgery more difficult, but may also leave possible complications, thus immediate radiotherapy should be kept for the rare case of acute onset SVCs with documented serious neurologic complications not due to cerebral metastasis.⁽¹²⁾

The diagnosis procedures used in clinical practice include both invasive and non-invasive procedures. Chest X-RAY is the most common investigation, and gives much information. CT scans of chest more clearly demonstrate the obstruction of the superior vena cava by extrinsic mass or intravascular

lesion, and it can be used as a guide for fine needle aspiration biopsy. The most frequent invasive procedure used in our services was FNA which had a high positive yield. Moreover, the FNA is not difficult to perform and has low complication rates. In contrast to Yellin A,⁽¹⁵⁾ the broncoscopic examinations were done infrequently and had low positive yield, however the reason was unknown. Mediastinoscopy, which was the most common and high-yielding procedure in Yellin A. series, was also infrequently done. Supraclavicular lymph node biopsy was also a useful diagnostic procedure, however there was a caution that an edematous supraclavicular fat pad or thrombosed vein can be mistaken for an enlarged lymph node.⁽¹⁶⁾ Complications in these various procedures occurred infrequently. Bleeding occurring during lymph node biopsy or thoracotomy was easily controlled. Recent studies have confirmed the low morbidity rate associated with the diagnostic procedures.^(12-14,17,18)

In general, the treatment of SVCs syndrome depends on the clinical situation in which it occurs. If the obstruction is acute, causing severe symptoms, or it is progressing rapidly, tissue diagnosis may be deferred and radiotherapy is the treatment of choice. Corticosteroids and diuretics have been tried under these circumstances, but we know of no controlled studies that justified their use and their value is probably limited to the acute situation⁽¹⁴⁾ ailment. Radiation therapy is one of major choices of treatments. It can be used either as a sole therapy or in combination with chemotherapeutic agents, the response rate seems to improve in our group treated with a combination of radiotherapy and chemotherapy as compared to previous study.^(19,20) The response to treatments also depends on the type of underlying

malignancy. Lymphoma, small cell cancer, and germ cell tumor are examples of chemosensitive malignancies which may respond well to chemotherapy, even it is used as a single treatment. While non-small cell-lung cancer, which is relatively chemoresistant, may have higher response in combination treatment programs. The chemotherapeutic regimens were selected by the basis of using high activity cytotoxic drugs in a particular disease, such as platinum-based chemotherapeutic regimens in non-small cell lung cancer. With proper management a high rate of symptomatic relief can be expected and even survival may approximate that of patients with similar diseases without SVCs.

In conclusion, SVC syndrome, mainly caused by malignant conditions of mediastinum should be considered as markers of local invasiveness of underlying malignancy. In general, SVC syndrome does not often cause a severe clinical outcome, thus we will have time to obtain an accurate diagnosis before starting specific treatments. To achieve the best outcome, the treatment modality could be considered according to both severity of symptoms and underlying pathology. The vast majority of SVCs patients respond to treatments and among the responders, the survival time is seen to be similar for those patients of the same disease without SVCs.

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