# Original Article

# An abnormal elevation of serum CA72-4 due to taking King Ratsnake meat in a healthy individual

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Abstract: Serum CA72-4 has been widely used as tumor marker in clinical treatment. It has been reported that some food, drug, or health promotion products such as ganoderma lucidum spore powder and colchicine can cause abnormal elevation of serum CA72-4 in different patients. In this case, a patient with abnormal elevation of serum CA72-4 level owing to having King Ratsnake meat was found in our laboratory. However, it was observed that the CA72-4 level was not elevated in the drug contained the snake ingredients and in respiratory disease patients who drank the drug made from the snake. It is speculated that having King Ratsnake meat may affect the detection results of serum CA72-4 from this report, which also suggests that clinicians could think of the case reported in our case when they have similar problems.

Keywords: CA72-4, King Ratsnake, health care individual

#### Introduction

Serum CA72-4 could be used to auxiliary diagnosis, monitoring and curative effect assessment in the management of gastric cancer, it is one of the most valuable tumor markers of gastric cancer as well as CEA [1-4]. However, its elevation was found in some other tumors including lung, pancreatic, ovarian and endometrium malignancies [5-8]. Therefore, CA72-4 has been widely used as tumor marker in clinical treatment. Recently, it has been reported that some food, drug or health promotion products such as ganoderma lucidum spore powder and colchicine can cause abnormal elevation of serum CA72-4 in different patients [9, 10]. CA72-4 elevation even was observed in type 2 diabetes patients [11]. Currently, there have been no reports about the effect of having King Ratsnake on serum CA72-4 level. King Ratsnake also latin named Elaphe carinata is one of the main genera of rat snakes, which occur in many regions of the northern hemisphere [12]. The case of a patient with abnormal elevation of serum CA72-4 level due to taking King Ratsnake is presented here. In addition, whether the CA72-4 level was elevated in the drug contained the snake ingredients and in respiratory disease patients who drank the drug made from the snake is evaluated.

### **Case report**

On April 1st, 2016, a 32-year young man came to our hospital for a regular routine health care including physical examination, routine laboratory tests, and imaging examination. The patient's physical examination showed no abnormal results including body temperature, pulse, respiration rhythm, blood pressure, and abdominal palpation. The patient had no history of chronic diseases and no physical abnormality only with regular physical examination. Abdominal ultrasonography and chest computed tomography showed the thickening of the lung texture without other abnormalities. Laboratory results showed that the CA72-4 level significantly increased (>300 U/mL; upper normal limit 6.9 U/mL). After dilution, the serum CA72-4 is 316.7 U/mL. Serum neuron specific enolase (NSE), triglycerides and cholesterol were slightly elevated. Other laboratory results including glucose, creatine kinase-MB (CK-MB), α1-fetoprotein (AFP), carcinoembryonic antigen

**Table 1.** Dynamic changes of the serum CA72-4 results in the patient (Reference Interval <6.9 U/mL)

Items	Date			
	Apr 1, 2016	Apr 4, 2016	Apr 14, 2016	Jul 20, 2016
CA72-4 (U/mL)	316.7	51.4	8.2	2.5

(CEA), CA19-9, CYFRA21-1, liver and renal function tests, etc., were within normal ranges. Of note, all of the tumor markers including AFP, CEA, CA19-9, CA72-4, CYFRA21-1 and NSE were measured by electrochemiluminescence immunoassays using the Cobas e602 automated analyzer (Roche, Basel, Switzerland). The analyzer was routinely maintained according to the manufacturer's instructions and standard operation procedure (SOP) of our laboratory. Dedicated reagents, which are from Roche Company, were used for measurement. Internal quality controls (IQC) products were from Bio-Rad Company and were performed by the Westgard multi-rules. In order to ensure the reliability of the test results, CA72-4 carried out second measurement and the result was same as before. The young man, who had no tumor history and no family history of tumor, felt very nervous and consulted a doctor in Medical Examination Center. After a doctor's careful inquiry, he remember that the dinner of last night had no difference with before only added a dish made of King Ratsnakes. The doctor speculated that it might be that food containing King Ratsnake meat that caused an abnormal increase in CA72-4. Considering the patients without other physical discomfort, only the CA72-4 was abnormal, so no further examination was carried out. To determine if the dish made of King Ratsnake meat could interfere with the CA72-4 assay, the doctor asked that in addition to not eating King Ratsnake meat, the others he has is the same as before. Careful consideration should be taken to prevent patients from suffering from cancer and to avoid the patient conditions worsen, he was asked to monitor serum CA72-4, regularly. In the next period of time, the CA72-4 had been performed in the patient for three times. The complete results are showed in Table 1. The results showed that the CA72-4 level of the patient decreased gradually and returned to normal level after three months. In details. serum CA72-4 of the patient decreased significantly (316.7 U/mL to 51.4 U/mL) after three days (Apr 1 to Apr 4), although it was still over the upper normal limit. The serum CA72-4 of the patient continued to decline, and returned to nearly normal level after 10 days. Delightingly, serum CA72-4 returned to normal level after three months.

To make effective clinical decisions, it is necessary to have appropriate reference intervals [13]. In addition, some substance that could interfere with the test of serum also needs to be paid more attention. Therefore, CA72-4 increased as a result of eating King Ratsnake meat should arouse our attention that some of the drugs which contain snake ingredients whether interfere with the CA72-4 assay.

To determine if snake product can interfere with the CA72-4 assay, the superiority way is to choose the other similar patients who eat King Ratsnake meat, and then detect their serum CA72-4. However, considering that someone has eaten the King Ratsnake meat and does not feel uncomfortable, he would not see a doctor in the hospital, thus it is difficult to find such patients. It is an alternative method that a Chinese Traditional Patent Medicine which contains the snake ingredients was selected for the detection of CA72-4. The drug named "She dan chuan bei oral liquid". The liquid drug is produced by the Shanghai pharmaceutical company. In addition to containing snake ingredients, it also contains other Chinese medicinal ingredients. This liquid drug is used to detect whether CA72-4 is elevated. According to the manufacturer's instructions, 2 ml drug were directly used for measuring and repeated detection for three times. The average of CA72-4 is 3.2 U/mL which is within normal limit (6.9 U/mL).

The drug is mainly used for adjuvant treatment of respiratory disease including cough and sputum. Therefore, 3 patients with pulmonary infection and cough were chosen who were treated with this drug. Serum CA72-4 of these patients was detected in second days after taking these drugs. The results of CA72-4 in the three patients were 2.4 U/mL, 1.6 U/mL and 2.0 U/mL, respectively. The detailed results of three patients are shown in **Table 2** and suggest that it has no effect on elevation of CA72-4 as an adjunctive treatment for respiratory system infection.

Table 2. Detailed CA72-4 results of three patients after drinking the drug containing the snake

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Patients ID	1	2	3
Enrollment date	Jul 7, 2016	Nov 24, 2016	20-Jul-18
Age (years)	62	61	50
Gender	Female	Male	Male
Disease	Pulmonary infection	Pulmonary infection	Pulmonary infection
Oral volume (ml/d)	30	30	30
Oral frequency	t.i.d.	t.i.d.	t.i.d.
CA72-4 (U/mL)	2.4	1.6	2

#### Discussion

To the best of our knowledge, this is the first case report about abnormal elevation of serum CA72-4 level which could be caused by having King Ratsnake meat. In this case, the patient is a health care individual who was only eating King Ratsnake meat without taking any other special food in the night before health care. It was deduced that serum CA72-4 elevation was attributable to have King Ratsnake meat. Moreover, it is concerned that whether snake drugs can affect serum CA72-4 and could lead to an erroneous clinical decision. Therefore, CA72-4 of the drug was measured for three times, the CA72-4 negative results also eliminated our concern. It also indicates that the drug itself does not affect detection of CA72-4. Furthermore, CA72-4 did not increase in three patients taking the drug. This shows that neither the drug itself nor the patients taking drugs have any effect on CA72-4.

Currently, it is as known that ganoderma lucidum spore powder and colchicine could cause abnormal elevation of serum CA72-4. Now, it can be speculated that having King Ratsnake meat may affect the detection results of serum CA72-4. However, this result also suggests that clinicians could think of this case report when they have similar problems. This should be explained to the patient after excluding various related diseases, especial a tumor.

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#### Disclosure of conflict of interest

None.

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#### References

- [1] Ychou M, Duffour J, Kramar A, Gourgou S and Grenier J. Clinical significance and prognostic value of CA72-4 compared with CEA and CA19-9 in patients with gastric cancer. Dis Markers 2000; 16: 105-110.
- [2] Jiang J, Xu N, Wu C, Deng H, Lu M, Li M, Xu B, Wu J, Wang R, Xu J and Nilsson-Ehle P. Treatment of advanced gastric cancer by chemotherapy combined with autologous cytokineinduced killer cells. Anticancer Res 2006; 26: 2237-2242.
- [3] Ebert MP and Röcken C. Molecular screening of gastric cancer by proteome analysis. Eur J Gastroenterol Hepatol 2006; 18: 847-853.
- [4] Jing JX, Wang Y, Xu XQ, Sun T, Tian BG, Du LL, Zhao XW and Han CZ. Tumor markers for diagnosis, monitoring of recurrence and prognosis in patients with upper gastrointestinal tract cancer. Asian Pac J Cancer Prev 2014; 15: 10267-10272.
- [5] Mariampillai Al, JPD C, Suh J, Sivapiragasam A, Nevins K and Hindenburg AA. Cancer antigen 72-4 for the monitoring of advanced tumors of the gastrointestinal tract, lung, breast and ovaries. Anticancer Res 2017; 37: 3649-3656.
- [6] Wang Z and Tian YP. Clinical value of serum tumor markers CA19-9, CA125 and CA72-4 in the diagnosis of pancreatic carcinoma. Mol Clin Oncol 2014; 2: 265-268.
- [7] Terry KL, Schock H, Fortner RT, Hüsing A, Fichorova RN, Yamamoto HS, Vitonis AF, Johnson T, Overvad K, Tjønneland A, Boutron-Ruault MC, Mesrine S, Severi G, Dossus L, Rinaldi S, Boeing H, Benetou V, Lagiou P, Trichopoulou A, Krogh V, Kuhn E, Panico S, Bueno-de-Mesquita HB, Onland-Moret NC, Peeters PH, Gram IT, Weiderpass E, Duell EJ, Sanchez MJ, Ardanaz E, Etxezarreta N, Navarro C, Idahl A, Lundin E, Jirström K, Manjer J, Wareham NJ, Khaw KT,

#### A case with abnormal CA72-4 elevation

- Byrne KS, Travis RC, Gunter MJ, Merritt MA, Riboli E, Cramer DW and Kaaks R. A prospective evaluation of early detection biomarkers for ovarian cancer in the European EPIC cohort. Clin Cancer Res 2016; 22: 4664-4675.
- [8] Anastasi E, Manganaro L, Granato T, Benedetti Panici P, Frati L and Porpora MG. Is CA72-4 a useful biomarker in differential diagnosis between ovarian endometrioma and epithelial ovarian cancer? Dis Markers 2013; 35: 331-335.
- [9] Zhao B, Zhang M, Xie J, Ren Y, Liang Y and Yang Z. An abnormal elevation of serum CA72-4 due to taking colchicine. Clin Chem Lab Med 2017; 56: e13-e15.
- [10] Liang Y, He M, Fan X, Ye W, Yang Z and Zhong R. An abnormal elevation of serum CA72-4 by ganoderma lucidum spore powder. Ann Clin Lab Sci 2013; 43: 337-340.

- [11] Shang X, Song C, Du X, Shao H, Xu D and Wang X. The serum levels of tumor marker CA19-9, CEA, CA72-4, and NSE in type 2 diabetes without malignancy and the relations to the metabolic control. Saudi Med J 2017; 38: 204-208.
- [12] Han H, Wu Y, Dong H, Zhu S, Li L, Zhao Q, Wu D, Pei E, Wang Y and Huang B. First report of hepatozoon (apicomplexa: adeleorina) from king ratsnakes (elaphe carinata) in shanghai, with description of a new species. Acta Parasitol 2015; 60: 266-274.
- [13] McCudden CR, Brooks J, Figurado P and Bourque PR. Cerebrospinal fluid total protein reference intervals derived from 20 years of patient data. Clin Chem 2017; 63: 1856-1865.