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APPLICATION NOTES

Copper/Zinc ratio: a useful indicator for differentiation of sarcoidosis from pulmonary tuberculosis and lung cancer

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Introduction

In clinical practice, it is usually difficult to differentiate sarcoidosis (*see below) from pulmonary tuberculosis and lung cancer. Various changes of sCu, sZn and sCu/Zn have been found in lung cancer and tuberculosis.¹⁻⁵ However, the diagnostic significance of sCu, sZn and sCu/Zn in sarcoidosis was not found in the literature. This study suggests that sCu, sZn and sCu/Zn can be used in the differential diagnosis of sarcoidosis from lung cancer and tuberculosis.

Subjects and methods

Fifty healthy persons (25 males and 25 females) were selected as controls, with ages ranging from 20 to 70 years. Diseased subjects included: fourteen cases (6 males and 8 females, aged from 16 to 32 years) of pathologically-proven pulmonary sarcoidosis; seventy-two patients (43 males and 29 females, aged from 16 to 78 years) with tuberculosis, proven by chest X-ray and detection of Mycobacterium tuberculosis in sputum; and eighteen cases of cancer (all males, aged from 22 to 75 years, including thirteen cases of squamous cell cancer, four cases of small cell cancer and one case of adenocarcinoma).

Blood samples were taken by venipuncture in the early morning after an overnight fast. Serum copper and serum zinc were determined using a GBC double beam atomic absorption spectrophotometer with an air-acetylene flame. The intra- and inter-assay variation coefficients were less than 3.6% both for sCu and sZn (n = 20). All results were expressed as $\bar{x} \pm SD$ (sample mean plus or minus 1 standard deviation). Statistical significance was assessed by Student's t-test. The concentration unit used is parts per million (equivalent to mg/litre).

Results

Mean concentrations of sCu, sZn and sCu/Zn in control and patient groups are shown in Table 1.

Examination of Table 1 shows no significant differences between sarcoidosis and control groups for sCu, sZn and sCu/Zn data. However, for the tuberculosis and lung cancer groups, sCu and sCu/Zn data were significantly higher, and sZn significantly lower, than corresponding data for the control group.

	sCu ppm	sZn ppm	sCu/Zn
Control	0.96 ± 0.17	1.06 ± 0.18	0.93 ± 0.11
Sarcoidosis	0.98 ± 0.30	0.98 ± 0.35	1.03 ± 0.23
Tuberculosis	1.28 ± 0.29	0.69 ± 0.17	1.98 ± 0.83
Lung Cancer	1.28 ± 0.43	0.58 ± 0.15	2.30 ± 0.79

Table 1: Concentration of sCu, sZn and sCu/Zn in control and patient groups (mean ± SD)

Figure 1 shows the relationship between sCu and sZn for each of the groups studied. Data for both control and sarcoidosis groups showed positive correlations, with coefficients of correlation, r, of 0.795 and 0.714, respectively. There was no correlation between sCu and sZn for the tuberculosis and lung cancer groups.

* Sarcoidosis is a disease of unknown cause, with lesions resembling those of tuberculosis. It affects the lungs and several other organs.

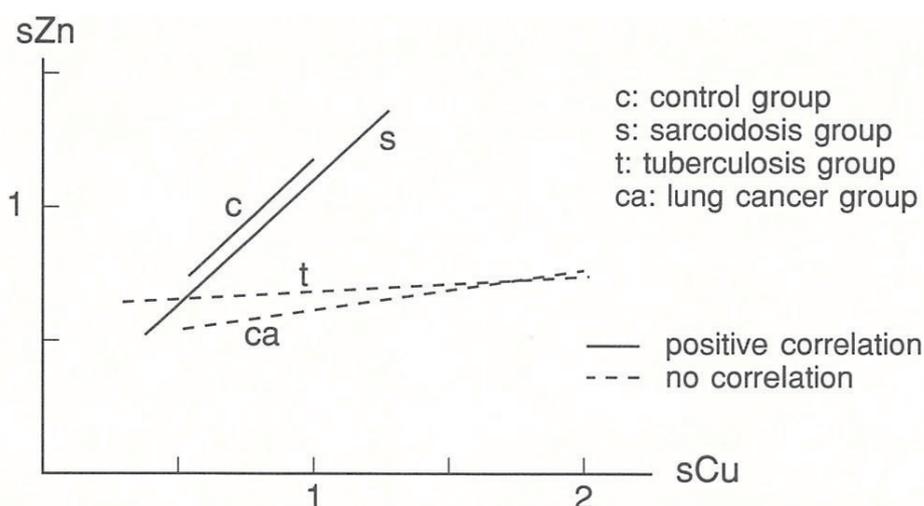


Figure 1: Relationship between sCu and sZn in control and patient groups

Discussion

Most cases of sarcoidosis show abnormal chest X-ray results and need to be differentiated from tuberculosis and lung cancer. In clinical practice, patients with sarcoidosis have been erroneously diagnosed as having lung cancer and received inappropriate surgical treatment. Currently, lung biopsy is considered a standard method for the diagnosis of sarcoidosis. Other methods include the use of serum angiotensin converting enzyme, examination of T lymphocytes in bronchoalveolar lavage, and lung scanning with gallium-67, but these methods are not specific, and each possesses some limitations. At present, with no ideal method for the diagnosis of sarcoidosis, new methods need to be assessed.

The concentrations of sCu and sZn for patients with tuberculosis or lung cancer have been studied for a long time and have been reported.^{1,3,4,5} It has been pointed out that elevated levels of sCu and decreased levels of sZn characterised these two diseases. The results in this paper confirmed these findings. Moreover, we found insignificant differences between the control and sarcoidosis groups for both sCu and sZn.

As criteria for the evaluation of individual subjects, we selected sCu of 1.2 ppm (mean + 2SD of control group), sZn of 0.8 ppm (mean – 2SD of control group) and their ratio of 1.5. The distributions of abnormal values of sCu, sZn and sCu/Zn for each group are shown in Table 2.

The significance of the above three criteria in the differentiation of sarcoidosis from tuberculosis and lung cancer is shown in Table 3.

	sCu > 1.2 ppm	sZn < 0.8 ppm	sCu/Zn > 1.5	sCu > 1.2, sZn < 0.8 and sCu/Zn > 1.5
Control	10.0	6.0	0	0
Sarcoidosis	28.6	35.7	0	0

Table 2: Distributions (%) of abnormal values of sCu, sZn and sCu/Zn in control and patient groups

The use of sCu/Zn < 1.5 as the criterion showed a sensitivity of 100%, specificity of 88.9% and accuracy of 93.8% for sarcoidosis versus lung cancer. The values for sarcoidosis versus tuberculosis were 100%, 73.6% and 77.9% respectively.

	sCu < 1.2 ppm			sZn > 0.8 ppm			sCu/Zn < 1.5			sCu < 1.2, sZn > 0.8 and sCu/Zn < 1.5		
	ST	SP	AC	ST	SP	AC	ST	SP	AC	ST	SP	AC
Sarcoidosis vs Tuberculosis	71.4	52.8	55.8	64.3	72.2	70.9	100	73.6	77.9	42.9	88.9	81.3
Sarcoidosis vs Lung Cancer	71.4	55.6	62.5	64.3	94.4	81.3	100	88.9	93.8	42.9	100	75.0

Table 3: Sensitivity (ST), specificity (SP), and accuracy (AC) of sCu, sZn, and sCu/Zn in the differentiation of sarcoidosis from tuberculosis

The use of sCu < 1.2 and sZn > 0.8 as the diagnostic criteria has its own merits, but these criteria were not as satisfactory as sCu/Zn. The combined use of sCu, sZn and sCu/Zn could get high specificity (88.9 or 100%), but the sensitivity and accuracy decreased markedly. Therefore the sCu/Zn ratio was better than sCu or sZn alone and also better than the combined use of sCu, sZn and sCu/Zn.

Other diseases can also cause changes in sCu, sZn and sCu/Zn, and normal values of sCu, sZn and sCu/Zn can also occur in conditions other than sarcoidosis. If patients were suspected of sarcoidosis clinically and there was a need to differentiate this condition from tuberculosis and lung cancer, the determination of sCu/Zn would prove helpful.

References

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