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葡萄胎曾患者家族癌症史研究

A Study of Family History of Cancer in Wemen with a History of Molar Pregnancy

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摘要 对1980～1981年间先后两次在广西灵山、钦州及扶绥县农村进行葡萄胎发病调查中获得的141例曾患者家族癌症史有关资料及1983年就葡萄胎曾患者家族癌症史问题在南宁市及其近郊进行的112例专题调查作综合研究。各项调查均同时在每例曾患者的同村庄，同街道，或同一工作单位随机选取1～2例年龄、胎次相当，且无自发流产或死胎史的曾孕妇女作为对照。结果表明，各组曾患者家族癌症史阳性率均高于对照组，以南宁组者为最高，达21.8%(22/101)；其中又以一级亲属所占的比例最高，与对照组相比，差异性显著（$P<0.05$)；调查涉及的癌，大多属多基因（或多因子）遗传癌。提出，葡萄胎可能有多基因（或多因子）遗传基础，且与其他多种癌有一部分共同的发病因素。对葡萄胎家族聚集性不明显的可能原因进了简短讨论。

关键词 葡萄胎 多基因（或多因子）遗传

Abstract An increase of the frequency of positive family history of cancer in women who had ever had a molar pregnancy was noted during investigations on the incidence of the disease conducted in counties Lingshan and Qinzhou (1980) and Fusui (1982) of Guangxi Zhuang Autonomous Region. Totally 141 molar cases were identified and interviewed with special reference to family history of cancer. The finding was further confirmed in Nanning, the capital of Guangxi, with an even higher frequency (21.8%, 22/101) found and more than two thirds of the family members with cancers of various organs in the molar group were first-degree relatives of the cases and/or their husbands. Controls were randomly selected from the same villege, street or working unit at the same time, at least one for each case. Most of the cancer involved in the investigations had been reported as polygenic (or multifactorial) ones. we believe that hydatidiform mole would probably also be of a polygenic basis and have a predisposing factor or factors in common with the other polygenic (or multifactorial) cancers. The reasons of why familial aggregation of hydatidiform mole itself had not been very common were briefly discussed.

Key words hydatidiform mole, polygenic (or multifactorial) heredity

An increase of the frequency of positive family history of cancer in women who had ever had a molar pregnancy was noted during the investigations on the incidence of hydatidiform mole(HM) in a number of the rural areas in Guangxi Zhuang Autonomous Region. This finding was further confirmed with another investigation designed for the subject in Nanning , the capital of Guangxi . Of particular interest was that in the molar group, eighteen of the twenty-four family members with cancer of various organs were first-degree relatives of the cases and/or their

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husbands. A question has then arised to us if there is any predisposing factor or factors in common with mole and other cancers.

1 Materials and Methods

we used findings from three investigations conducted successively in 1980, 1981 and 1983[1~3]. Data were collected from structured interviews. One or two controls who matched both in age (within 5 years) and in number of pregnancies (into four groups: 1, 2, 3~5 and >5 pregnancies) and had no history of spontaneous abortion or intrauterine fetal death were randomly selected from the same village, street or working unit at the same time, the same questionaire being used, for each moler case found.

The interviews in rural areas in the first two investigations were mostly performed by the primary-unit medical personel or women cadres who had been given a relevant short training previously. The questionaires handed back were checked carefully by us before accepted, and a small number of the objects were reinterviewed by ourselves, in order to check the general reliability, the diagnosis was mostly established on gross specimen of curettage.

A total number of 20548 fertile women in two counties, Lingshan and Qinzhou, were interviewed in 1980. Eighty-six of them were found to have a history of mole, and eighty-two among the eighty-six had available data on cancer family history and matched controls. During the investigation of the next year, 23336 fertile women in Fusui, another county, where liver cancer had been highly prevalent , were investigated, and seventy-six had a molar pregnancy; fifty-nine of the seventy-six had had relevant available data and matched controls. The investigation in Nanning was conducted in 1983. One hundred and twelve women, who had been living in the urban districts or suburbs and had been once admitted as patients with mole in one of the twelve hospitals in the city during 1978~1982, were sought out with the hospital records, and identified and then interviewed in their home or working unit by us. Each positive reply of cancer family history was strictly checked , only those with the diagnosis of cancer made at a hospital were included. One hundred and one out of the one hundred and twelve provided a clear data of family history on cancer , with matched controls available as well.

2 Results

2.1 Frequency of cancer family history

As shown in table 1, the frequency of cancer family history was apparently higher in the molar cases in all of the three different groups, the highest being as high as 21.8% (22/101).

2.2 Frequency of positive cancer history in first-degree relatives

Among the 22 cases with a family history of cancer in Nanning group, 17 cases had a cancer history in their first-degree relatives, making up a frequency of 16.8% (17/101), more than two thirds of the total frequency of 21.8% while the corresponding figure of the control group was 5%. The difference between the two was statistically significant at $P < 0.05$ (Table 2).

Table 1 Frequency of positive cancer family history of the three molar groups and their matched controls

Group		Total cases	Cases with positive cancer family history
Lingshan Qinzhou	HM	82	6 (9.8)
	control	117	1 (0.9)
Fusui	HM	59	10 (16.9)
	control	59	4 (6.8)
Nanning	HM	101	22 (21.8)
	control	101	9 (8.9)

Data in brackets are percentages.

Table 2 Frequency of cancer history in first-degree relatives of the 101 molar cases in Nanning group and their matched controls

Group	Total cases (n)	Cases with cancer family history	
		Tatal	With cancer history in 1st-degree relatives
HM	101	22 (21.8)	17 (16.8)
control	101	9 (8.9)	5 (5.0)

Data in brackets are percenfages. $P < 0.05$.

2.3 The cancer-affected relatives and the sites of cancer

In the two groups of Lingshan and Fusui, the affected relatives included parents, brothers or uncles of either the cases or their husbands, and in addition one molar case's husband and another's son were also included. The site of cancer included the liver, breast, stomach and uterine cervix, and most of them were liver cancers, i.e, 7 out of 10 in the molar group and 3 of 4 in the controls, in Fusui county probably because of the unusually high prevalence of liver cancer there. The cancer-affected rela-

tives in Nanning group were similar to that of the other two groups in the concrete relationships but also found in paternal or maternal aunts, a maternal grandfather and a step-father. There were altogether twenty-four of them in the molar group. Eighteen of the twenty-four were first-degree relatives of the molar cases. The relevant data and the sites of cancer involved in Nanning group were listed in table 3.

As shown in table 3, all the cancer-affected first-degree relatives were parents or parents-in-Law. There was one molar case who had two cancer-affected first-degree relatives, both her mother and father-in-Law had died of cancer. Another molar case also had two cancer-affected relatives, though not first-degree ones. There was still another molar case, whose mother had had a uterine myoma and one of her maternal aunts had had an ovarian cyst (considering that both myoma and ovarian cyst are generally not malignant, she has not been included in the 22 cases). No one in the control group had more than one cancer-affected relatives.

Liver cancer again made up a considerable part of the cancers in this group. The other cancer sites included the lungs, stomach, bowel, esophagus, uterus and so forth (Table 3).

Table 3 The affected first-degree relatives and the sites of cancer in Nanning group

Site of cancer	Affected 1st-degree relatives							
	Father		Mather		Father-in-law		Mather-in-law	
	HM	control	HM	control	HM	control	HM	control
Liver			1		4	1		
Lung	2							
Stomach	1				2			
Bowel	1				1			
Esophagus			1				1	
Uterus			1					
Nasopharynx	1	1						
Brest			1	1				
Urine bladder					1			
Lymphatic		1						

3 Discussion

It seems there do exists certain internal association between HM and other cancers as revealed by the significantly higher frequencies of cancer family histoy in women who had ever had a molar pregnancy in all of the three different groups presented. The relation between HM and other tumors would become more striking if considering those who had even more than one relatives affected by tumor, either malignant or benign, in the molar group. In Nanning group, the interviews were carried out by the authors themselves and the frequency of cancer family history is higher than that in the other two groups. The most probable explanation for this, we believe, would be that quite a number of patients with cancer would get no chance to have their disorders diagnosed or correctly diagnosed in the rural areas because of the limited medical and health survices there especially during the days that the investigations were conducted, though the possibility of certain degree of carelessness or roughness in work with the primary-unit personnel who had taken part in the interviews could not be completely excluded. Even in Nanning group, there might be quite a number of individuals whose parents or other relatives had been living in rural areas for long and thus it might be reasonable to estimate that the figures listed above would still be lower than real.

Most of the cancers involved in the investigations, such as the hepatic, pulmonary, gastric, intestinal, nasopharyngeal, mammary and uterine, had all been reported as polygenic (or multifactorial) in origin. One of the family features of a polygenic (or multifactorial) disease is that "The frequency of occurence in the first-degree relatives of the affected individuals is higher than that in population and the frequency decreases with decreasing relationship." The data listed above are quite consistent with these feature. So the possibility for HM being a polygenic (or multifactorial) disease as well deserves serious consideration. In addition, as repeatedly reported in the literature, HM recurred frequently, even up to more than ten times in a small part of patients with the disease. This outstanding but up-to-date unexplained clinical feature of HM can just be well explained with another character of polygenic diseases: "The frequency of recurrence in the next sibling increases with increasing number of affected children" or, in other words, "There is an increased risk of recurrence after two affected children."

Now could we soppose that HM is also a polygenic (or multifactorial) disease which has a part of predisposing genes (or factors) in common with the polygenic tumors involved in the investigations and therefore exhibits familial charactors in common with them. Could we then deduce still further that there might be certain basic predis-

posing gene or genes in common with all tumors , including both the malignant and the benign ones, and every different tumor has it's own characteristic genes or environmental factors in addition.

Another phenomenon seeming to be consistent with the supposition was noted in Fusui where altogether seven communes were investigated. The lowest incidence of HM among the seven communes occurred in that one where the incidence of liver cancer and the incidence of malignancies in all were also the lowest while it was not true for the highest incidence of them (Table 4).

Familial aggregation of HM itself is not so common as a genetic tumor usually exhibits though there do have been a few number of sporadic cases reported in the literature. This perhaps might be explained by the followings: (1) HM can only occur in pregnant women; (2) the diagnosis can be missed in a number of early spontaneous abortion; (3) the mole itself can't survive and reproduce; (4) according to the well known theory of androgenesis, the development of HM would in quite a great measure depend on paternal factor; these would greatly reduce the chances for the disease to reccur in a same family.

Table 4 Distribution of incidence of HM in comparison with mortality of liver cancer and mortality of malignancies in all in seven communes of Fusui county

Name of commune	*Mortality of all malignancies (1/100 000)	*Mortality of liver cancer (1/100 000)	Incidence of HM (1/100 000 wemen)
Quli	101.54	63.22	273
Bapan	84.14	59.55	290
Zhongdong	72.06	51.04	395
Changping	71.95	62.96	142
Longtou	71.76	41.00	206
Funan	71.43	42.04	534
Liuqiao	52.68	39.51	137

* From *Fusui Liver Cancer Research*, 1979

According to a vast majority of relevant reports in the literature, there are two peaks of age incidence of HM, one before 30 and the other after 40 years , the later being higher than the former one. Whether the phenomenon implicates heterogeneity and the lower peak before 20 represants a genetic type of the disease also deserves consideration.

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