

PERSONAL RESEARCH REGARDING THE PARANEOPLASIC SYNDROMES ASSOCIATED TO THE BRONCHOPULMONARY CANCER CASE PRESENTATION

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Cuvinte cheie: Tromboflebite migratorii, degete hipocratice, sindrom reumatoid
Keywords: thrombophlebitis migrans, hypocratical fingers, rheumatoid syndrome

Rezumat: Prezentul articol își propune să demonstreze prezența mai multor sindroame paraneoplazice la același pacient, prezența lor fiind un factor de prognostic negativ, cât și diagnosticarea bolii pulmonare după apariția sindroamelor paraneoplazice. Datele existente în literatura de specialitate, în legătură cu rezistența tromboflebitelor la anticoagulante, au fost confirmate și în cazul nostru

Abstract: The present study proposes to demonstrate the presence of several paraneoplastic syndromes at the same patient, their presence being a negative prognosis factor even if the diagnosis of the pulmonary disease is set after the apparition of the paraneoplastic syndromes. The data in the specialty literature regarding the resistance of the thrombophlebitis at the anticoagulants drugs have been confirmed in our case.

INTRODUCTION

The paraneoplastic syndromes may precede the clinical manifestations of cancer. To establish a precocious diagnosis we need to know the clinical manifestations. The symptoms may appear at once with the clinical exteriorization of the tumour or in any other moment of evolution. Regarding those conditions, the paraneoplastic syndrome may prevail the clinic manifestations and the neoplasia may be ignored, leading to diagnosis and treatment mistakes. When the syndrome appears during the evolution of an already known cancer, it may be wrongly considered to be in connection with a metastasis, that may determine severe mistakes. (3) The paraneoplastic syndromes may appear in the final phase of the cancers, when they represent the direct cause of the patient's death and when recognising them would allow the application of a correct symptomatic treatment, that would prolong the patient's survival or at least would diminish the patient's suffering that represents in the incurable cases an important gain.

OSTHEOARTICULAR MANIFESTATIONS. DIGITAL HYPOCRATISM is the most simple aspect of those paraneoplastic syndromes. Clinically, hypocratical fingers have two characters: a longitudinal incurvation, transversal or mixt of the hand nails and leg nails; hypertrophy of the last phalanx pulp, firm, flexible, with a pink burelet. Around the nail, a discrete sweating may be associated on the palm of the fingers and inconstantly local cyanosis.

Those anomalies affect all the nails of the hand but predominantly the thumb, the index, the ring finger. The modifications also appear in the leg's nails, but aren't so obvious. This is the aspect that is the most frequently met in the bronchopulmonary cancers. Approximately 35% of the patients with bronchopulmonary cancer present digital hypocratism (5), but in a 3-4% of the patients it represents the inaugural symptom, preceding with a period of few months to two years the apparition of the thoracic manifestations.

PARANEOPLASIC "RHEUMATISMAL" SYNDROMS:

represents, sometimes, dissociated forms, deficient or degraded of osteoarthopathy. Those syndromes appear as a polyarticular chronic or subacute rheumatism, bilateral and symmetrical, inquiring especially the large, distal joints and rarely the small finger's joints. The patients present joints pain, periarticular moderate edema, rarely liquidian collection (in a 10-15% of the cases, especially the knees)(3).

HYPERTROPHIC PULMONARY OSTEOARTHROPATHY: is the best individualised syndrome, that was described in 1890 by Pierre Marie and concomitantly by Bamberger.(3) It has been observed in the intrathoracic cancers, especially in the bronchopulmonary and plural mesotheliomas. In 70-90% of the cases is secondary to the primitive or secondary pulmonary cancers. The frequency of the bronchopulmonary cancer varies from statistics to statistics, with an average of 3-5%. In 80-90% of the cases is associated with pulmonary cancer without small cells.(5)

The complete form has: digital hypocratism (that may be the only paraneoplastic manifestation); the excessive growing of the soft tissue of the extremities with vasomotori disturbances at this level (excessive perspiration and/or cyanosis); pseudoreumatoid syndrome manifested through pain and articular tumefactions (including synovitis), symmetrical at the fist articulations, knees or ankle; excessive subperiosteal bone formation, especially at the level of the long bones (femur, tibia, fibula, radius) evidenced better on the radiography. (2)

The disorder would consist of an increasing of the sanguine flow in the extremities, with the dilatation of the arteriovenous anastomosis, that determines a regional hypertrophy.(4)

CARDIO-VASCULAR MANIFESTATIONS. TROMBOPHLEBITIS *The association between thrombophlebitis and cancer was described, for the first time, in 1865, by Trousseau (59).* The presence of the typical lesions of migratory thrombophlebitis, with rare exceptions, may be

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established precisely that is pathognomonic for a visceral cancer. It is associated, especially, with mucous adenocarcinomas, the pancreatic cancer being the most frequent. And other tumours may be responsible for the production of those paraneoplasias: breast, ovarian, pulmonary, prostate, gastric.

Migratory thrombophlebitis is characterized by the presence of the recurrent venous thrombosis and the atypical localisation, accompanied, occasionally, of local inflammatory signs, leucocytosis and the increasing of the VSH.(1,3)

Those thrombophlebitis have two characters that allow their recognition, although they are not absolutely pathognomonic and specific: the migratory tendency, realising the picture of subacute venous septicemia of Vaquez; inefficiency of the anticoagulants.

CASE PICTURE

Patient aged 52 years, from urban environment, presents in the Emergency, with pains, of great intensity, at the level of the the radiocarpic joints, metacarpo-phalangeale and inter phalangeale proximal bilateral joints, with marked swollen at the level of those joints, left lateral toracic pains.

From the familiar antecedents we mention that his father died at the age of 54 years because of a bronchopulmonary cancer . From the personal pathologic antecedents we retain hepatic steatosis of II degree.

The history of the disease: patient aged 52 years, smoker, approximately 40 cigarettes a day present, of almost 3 months, left lateral toracic pains of high intensity, that constitute a reason for presenting several times to the doctor. A pulmonary radiography, a cardiologic consultation that haven't evidenced pathological modifications. Associated, in the last two weeks, presents pain at the level of the both hands joints with swelling, and functional impotence, reasons that bring him to the Emergency being hospitalised on the I st Medical Clinic of the County Clinical Hospital of Sibiu.

Objective examination: the clinical state is mediocre, teguments and pale mucosas, with swellings of the hand's fingers, hypocratic fingers .

Biological assays that were effectuated have proven: leucocytosis (L=18500/mm³) with neutrophilia (14200/mm³), marked thrombocytosis (Tr=520000/mm³), anemia syndrome (Hb=10,2g/dl, Ht=36%, with normal erythrocytosis index), biologic inflammatory syndrome (VSH=78mm/h, PCR=36 mg/dl, fibrinogen=540 mg%), Rheumatoid Factor present, hepatocyte syndrome, the rest of the assay being in normal limits.

It has been effectuated a thoracic radiographic that evidenced an inhomogenous opacity of medium intensity, left parahilar of approximately 4/5 cm; with a pronounced left hilum reaction. It is decided to continue the investigations with: thoracic computed tomography, that confirmed the supposition of bronchopulmonary cancer, and evidenced secondary left pleural determinations. The patient was transferred at the Hospital of BronchoPulmonary diseases of Sibiu to effectuate the bronchoscopy, that distinguished the histopathologic type: carcinoma with small cells in the first day of presentation in the Hospital of Pulmonary Diseases the patient presented important pains in the right calf with edema, heat at this level ; it has been effectuated a Doppler ecography that distinguished extended thrombosis in the femoro-popliteal axis. It has been initiated anticoagulant therapy and chemotherapy specific to the histopathologic type with favourable evolution during the first two months of treatment: the latero thoracic pains have been remitted, but persisted a certain degree of a postthrombotic syndrome at the right calf. At

approximately two months from the beginning chemotherapy, it is diagnosed a thrombophlebitis at the level of the right humeral vein, that didn't remitted at the administration of anticoagulants. At the end of the six months of chemotherapy with unfavourable evolution, with the persistence of the venous thrombosis, even their extension at the left calf , despite the administration of the anticoagulant therapy.

Further the evolution is unfavourable with the death of the patient at approximately 9 months from the diagnosis of the disease.

CONCLUSION

1. The initial presentation , at the doctor was registered as a rheumatoid syndrome, sustained, ulterior, by the modified biological assays the final diagnosis was that of bronchopulmonary cancer with small cells .
2. The rapid apparition of the profound venous thrombosis, the resistance at anticoagulants that didn't remitted under chemotherapy treatment .

The case particularity: the presence, concomitently, at several types of paraneoplastic syndromes: profound thrombophlebitis, rheumatoid syndrome , hypocratic fingers , normochromic, normocytic anaemia.

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GASTRIC CANCER IN PATIENTS \geq 75 YEARS

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Keywords: gastric cancer, laparotomy, elderly patients

Abstract: The aim of this study was to clarify whether gastric cancer in elderly patients warrants surgical resection of 300 patients with laparotomy for gastric cancer, 33 were older and 267 were younger than 75 years (control group). Mortality, morbidity, clinico-pathological features, and survival were compared between the two groups. There were no significant differences in mortality, 5 – year survival rate and morbidity between the two groups (elderly 2,9%, 36, 1% and respectively : control 0,7%, 24, 6%). Death from other diseases was 38,5% in the elderly group, and 9,1% in the control group. Conclusions: Gastric cancer in elderly patients warrants surgical resection, the benefits in early and long-term outcomes are the same as for younger patients.

Cuvinte cheie: cancer gastric, laparotomie, pacienți vârstnici

Rezumat: Scopul studiului actual a fost să clarifice, dacă rezecția chirurgicală la pacienții vârstnici cu cancer gastric este justificată. Din 300 de cancere gastrice laparotomizate, 33 au fost \geq 75 de ani, pe când 267 au fost mai tineri. Au fost comparate între cele două categorii mortalitatea, morbiditatea și trăsăturile clinico-patologice. Nu au fost observate diferențe semnificative în mortalitate, morbiditate și în supraviețuirea la 5 ani între cele două categorii de vârstă (vârstnici: 2,9%, 36,1%, control: 0,7%, 24,6%). Mortalitatea din cauza acestor afecțiuni comorbide a fost de 38,5% la vârstnici și 9,1% la grupul control. Concluzie: La pacienții vârstnici cu cancer gastric, este justificată rezecția, întrucât beneficiul privind supraviețuirea de scurtă și lungă durată este comparabil cu pacienții tineri.

INTRODUCTION

The number of gastric cancer patients \geq 75 years is increasing, despite a plateau in the total number of gastric cancer patients (1, 2). Some studies have shown higher mortality and morbidity rates in older patients after gastrectomy (2, 8, 9). Remains to be clarified how many of these patients die from diseases other than gastric cancer (11, 12, 13). The resection for gastric cancer in elderly patients is a matter of controversy (2 – 10).

THE AIM OF THE STUDY

The aim of this study was to clarify whether gastric cancer in elderly patients warrants surgical resection of 300 patients with laparotomy for gastric cancer, 33 were older and 267 were younger than 75 years (control group).

MATERIAL AND METHOD

From January 1980 through December 2004, 300 patients (204 men and 96 women) with gastric cancer underwent laparotomy. 75 years was used as the cut – off age between groups. In the study patients 33(11%) were \geq 75 years (elderly group) and 267 (88%) were \leq 74 years (control group). Pathological data were obtained from the pathologists. Mortality was defined as death within 30 days of surgery. Overall and disease specific survival rate was calculated using Kaplan – Meier method, the independent Student's t – test was used for the differences between groups, the Log Rank test was used to evaluate differences in survival.

RESULTS

The mean age was 60, the average age of the elderly

and control groups was 78 (range 75 – 85 years). In tables 1 and 2 significant differences between groups were observed with regard to lymph node involvement, metastasis, lympho-vascular invasion, depth of invasion, surgical method, histologically differentiation.

Table no. 1. Clinical features of the study group

	Elderly group (33)	Control group (267)	p
Operative method			
Total gastrectomy	12 (36,8%)	109 (41%)	0,
Subtotal gastrectomy	17 (52%)	151(56%)	11
Other resection	3 (5%)	2 (1%)	
Bypass or exploration	1 (2%)	1 (0,7%)	
Comorbidity:			
NO	20 (61%)	211 (76%)	0,
YES	12 (38%)	57 (23%)	07
Cardiovascular	4	27	
Respiratory	1	7	
Diabetes mellitus	3	8	
Others	4	15	

The morbidity rate was 36% in the elderly group and 24% in the control group, and the postoperative death within 30 days 2,9%, respectively 0,7%. The most common cause of morbidity in the elderly group was pneumonia (16%), the surgical in situ infection was the most important cause in the control group.

One patient died 15 days after operation because of progressive gastric carcinoma. Two patients in the control lot: one of progressive gastric carcinoma and one of myocardial infarction. In the study population, in elderly group 61,5% death

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from gastric cancer complication (peritoneal and liver metastasis, local recurrence), 38,0% death from other disease, and in control group 90% death from gastric cancer complications, 9,0% from other disease.

Table no. 2. Histopatological features of the study population

Elderly group (≥ 75 years) no = 33		Control group no = 267	p
Stage:			
IA	1 (3,3%)	2 (0,7%)	
IB	2 (6,6%)	6 (2,2%)	
II	5 (13,9%)	46 (17,2%)	
IIIA	11 (36%)	113 (43%)	
IIIB	9 (27%)	70 (21,9%)	
IV	5 (13,9%)	40 (16,1%)	
Topography:			
Proximal	7 (22%)	45 (16,8%)	0,1
Middle lower	8 (25%)	92 (34,4%)	
Lower	15 (47%)	107 (40,0%)	
Difuse	3 (5,5%)	23 (8,6%)	
Depth of invasion:			
Early (pT ₁)	1 (3,3%)	1 (2,6%)	
Advanced (pT _{2,3,4})	32 (96%)	266 (97%)	
Differentiation:			
Differentiated	19 (60%)	140 (52,4%)	
Undifferentiated	14 (40%)	137 (47,5%)	
Lymph node metastasis:			
Positive	29 (90%)	245 (91,7%)	
Negative	4 (10%)	22 (8,2%)	
Distant metastasis - Peritoneum:			
Positive	6 (20%)	43 (16,1%)	
Negative	27 (80%)	224 (83,8%)	
Distant metastasis - Liver:			
Positive	4 (13%)	34 (12,7%)	
Negative	29 (87%)	233 (87,2%)	

DISCUSSIONS

There is a perception that gastric cancer in older patients is more aggressive and advanced compared with in younger patients (2 – 8 – 14). Havazaki (8) reported that patients ≥ 80 years, had more advanced disease (60% versus 28% in younger patients) and larger tumors. In our study the rate of early gastric cancer is low (3,5% respectively 2,6%), but was not statistically different. The Japanese publications show that elderly patients do not present with more advanced disease and aggressive tumor biology (2, 9, 17). The mortality and morbidity rates of the elderly group was 2,9% and 3,6% respectively whereas for the control group, they were 0,7% and 24% respectively. These results show that age alone should not be considered a reason for not pursuing surgery for elderly gastric cancer patients. This study compared the surgical outcomes of patients ≥ 75 years of age with those of younger patients. The overall 5 years survival rate is significantly lower, whereas deaths from comorbidity is significantly higher among elderly patients. In general, the prognosis it's worse in elderly cancer patients, because of the mortality resulting from comorbidity. Past literature has reported that deaths caused by other diseases where 34% to 37% of deaths were among elderly patients (2, 17). On our series 38% of the deaths in elderly patients was caused by other diseases. This one is the reason for the poor prognosis in elderly patients with gastric cancer. The mortality rates of older patients (≥ 75 years) it's bigger after extended lymphadenectomy than those with limited surgery (14, 18).

CONCLUSIONS

In the present study elderly patients did not present with more aggressive and advanced carcinoma of the stomach. The poor prognosis was shown to be the high incidence of other diseases seen as comorbidities. In our opinion, elderly patients are warranted the surgical resection because the benefit is the survival.

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