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Research Article

WHICH TREATMENT FOR TPO (PRIMITIVE OCCULT TUMORS)

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ABSTRACT

Occult primitive tumors constitute 2-5% of adult neoplasms with an average age of onset of 60 years, in the US 31,000 new cases of TPO annually with a tendency to decrease the last 5 years. (1)The site of the tumor is identified only in 30% of cases, and even in the autopsy in 50% of cases it is not possible to reach the original site. The purpose of the study is to evaluate in relation to the clinical observation which is the most suitable therapeutic program that can offer a long survival associated with a dignified quality of life. **Materials and methods:** From January 2007 to December 2017 consulted database of departmental surgery of the AOU Polyclinic University of Catania, 32 cases of TPO (primary occult tumor) were observed. We have considered occult all those cases in which the tumor origin has not emerged from the usual diagnostic investigations. The surgical intervention was limited to those cases in which the clinical onset was dramatic (obstructive uropathy, intestinal obstruction) as the opportunity of resectionin the presence of multiple lesions does not find indications, as well as it is always a palliative intervention. Chemotherapy was the most interested therapeutic measure with a positive response that ranged from 10% to 35% -40%. **Results** Surgery for TPOs has found indications even if palliative in segmental gut resection (5 cases) with extensive mesentery resection and with hepatic MTS that were grouped into a single limited number lobe in the absence of other repeats in other locations and with exeresis in a single surgical time. chemotherapy after research and histological confirmation of metastatic ca to occult site, provided a protocol with pharmacological associations such as: 5- fluoro uracil ,adriamycin ,mitomycin C, Cisplatin. Paclitaxel **Discussion** A problem that unfortunately still hinders the spread of molecular targets is also their high cost, their use on different tumors can and will contribute to reducing the costs in addition to the market competition between the various pharmaceutical companies that they are developing these drugs. the cancer therapy that is very useful for these patients is still based on the oncologist's experience since there are no randomized clinical trials. surgical resection in association with palliative pharmacological printouts have achieved median survival of 12.3 months. **Conclusions** TPOs require careful evaluation in each case. the current literature expresses conflicting opinions that tend to dissuade the prolonged treatment, even though it is evident that immunomodulatory drugs pose a cautious optimism in the treatment of neoplasm. the definition of the histological type of the tumor remains the fundamental moment of the therapeutic strategy and the immunohistochemistry in association with the tumor's genetic profile have been confirmed essential to the achievement of the diagnosis

INTRODUCTION

Occult primitive tumors constitute 2-5% of adult neoplasms with an average age of onset of 60 years, in the US 31,000 new cases of TPO annually with a tendency to decrease the last 5 years. (1)The site of the tumor is identified only in 30% of cases, and even in the autopsy in 50% of cases it is not possible to reach the original site. the prognosis in these patients is evaluated by both negative prognostic factors such as: metastasis, male gender, ascites, ch3 by positive prognostic factors such as: female sex, the poorly differentiated, stotype, the lymph node only metastases, the poorly differentiated neuroendocrine tumors, and the PSA elevated. In 59% of cases, TPOs manifest with widespread disease. Patients then with

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favorable prognostic factors have an average survival of 12 to 36 months. The TPOs can be divided and cataloged into two main groups referring to the histological examination in NOS (unspecified adenocarcinoma,) and SSC (squamous carcinoma). A Swedish study showed that the origin of TPOs would be genetic in nature with a percentage 2.8% of the observed cases, associated to a family incidence of colorectal, pulmonary and renal tumors, for which they suggest in the first instance that diagnostic research is to be oriented in these devices, (2,3). The clinical strategy has as its primary objective a sure histopathology diagnosis, whereby the determination of the biomolecular markers associated with the anatomical site orientates the site of origin of the tumor. The difficulty of the nosological classification, the complex and long-term clinical management, the heterogeneousness of the morbid pictures has distinguished over time different occult forms: primitive, the similar primitive, (due to an incomplete study) and partially primitive (in which the study necessarily involves biological investigations). In addition to these tumors is also associated with vague, modest and non-specific symptoms.(4,5) The aim of the study is to evaluate in relation to the clinical observation which is the most suitable therapeutic program that can offer a long survival associated with a dignified quality of life

MATERIALS AND METHODS

From January 2007 to December 2017 consulted database of departmental surgery of the AOU Polyclinic University of Catania were observed 32 cases of TPO (occult primitive tumor). We have considered all those cases in which the cancer origin has not emerged from the usual diagnostic investigations with certainty. In the objective detection of MTS from occult tumor the histopathological study, which was not limited to definition, but was associated with immunohistochemical research, of cellular and cytogenetic biology, identified 4 histological groups: A) Poorly differentiated adenocarcinomas (20%) B) Well-differentiated adenocarcinoma (70%) C) Poorly differentiated epithelial Ca (neuroendocrine) (7%) D) Anaplastic Ca (3%).The diagnosis of MTS was achieved by surgical biopsy of the lymph nodes or needle aspiration of the lesion that in addition to guiding the first level diagnostic investigations (tumor markers, endoscopy, urography, Rx thorax, CT scan) were performed in the presence of clinical or biological signs of orientation The instrumental and laboratory tests had the primary objective of revealing both the primary tumor, for which curative treatment is still possible, and to determine how useful it is for the patient to prolong the research before starting a suitable therapeutic treatment. For sex distribution, 65% were male and the remaining 35% female. Patients were histologically studied by age group (52-62) and (72-82). Therefore, a therapeutic diagnostic strategy was created in which the occult MTS were dealt with in a multi disciplinary effort essential to accurately select the II level diagnostic tests useful to obtain more information with the minimum cost. The choice favored the II level examination such as: PET and RNM in addition to the CT already performed photo 1-2,

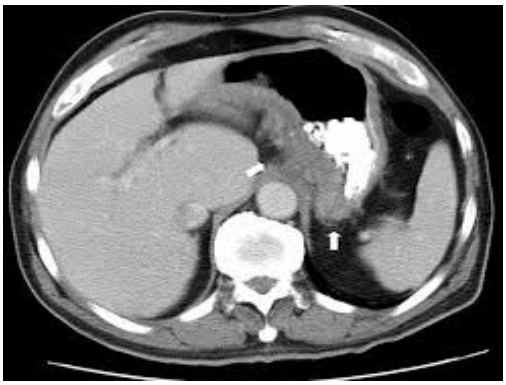


Fig 1 Ct abdomen sup MTS hepatic

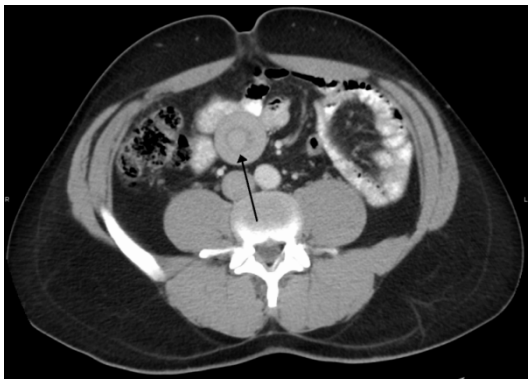
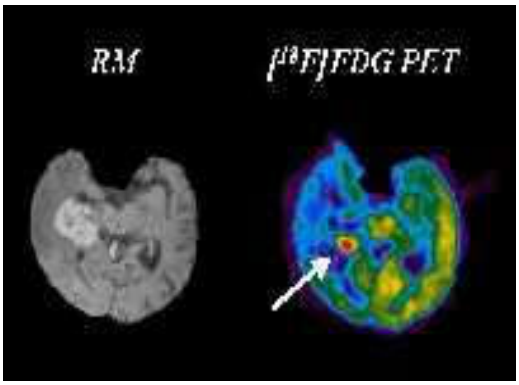


Fig 2 ct pelvis Mts vetebral column.

In order to obtain a quick identification of the primary office (in 70% of cases) avoiding unnecessary loss of time and money. The indications for the diagnostic tests for the research of MTS in relation to the histological diagnoses were: Localization of above clavicular lymph nodes, axillary lymph nodes, mediastinum and lung, pleural effusion, hepatic localization, bone, encephalic, multiple diffusion with skin involvement, inguinal lymph nodes. Finally, the radiologist's long experience has been of great help. The histopathological study in poorly differentiated adenocarcinoma showed that tumor growth was rapid in the presence of young (52-62 years) and male prevalence patients. The rapid evolution determined involvement of the retro peritoneal lymph nodes with sometimes dramatic clinical onset with the presence of an obstructive uropathy or occlusive crisis or signs of encephalic involvement. The cytoarchitectonic morphology was not sufficient to identify the primitive site, therefore immunohistochemistry was indispensable with the use of the ck20 antibody that allows to distinguish the gastrointestinal mts from the others, associated with the CK-7 antibody that marked different types of glandular epithelium and with a combination of them allowed to reach the diagnosis. In the well-moderately differentiated carcinomas that accounted for 70% of our observations, the pathognomonic clinical signs of a migratory peripheral vasculopathy were present above all in the group of elderly patients (72-82 years with multiple-disease). in the remaining 10% this group consisted of anaplastic ca, and poorly differentiated epithelial ca and neuroendocrine tumors. Also in these three groups it was possible to obtain the diagnosis, thanks to the PET / dotatoc in which the metabolic processes are measured and evaluated in vivo by means of radionuclides that allow to localize small lesions. Photo 3



MRI and MTS encephalic PET

The surgical intervention was limited to those cases in which the clinical onset was dramatic (obstructive uropathy, intestinal obstruction) because the opportunity of resection in the presence of multiple lesions is not indicated, besides it is always a palliative intervention. it was the most affected therapeutic provision with a positive response ranging from 10% to 35% -40%.

RESULTS

Surgery for TPOs has found indications even if palliative in segmental gut resection (5 cases) with extensive mesentery resection and with hepatic MTS that were grouped into a single limited number lobe in the absence of other repetitions in other sites and with resection in a single surgical time. In the neuroendocrine tumors the presence of localization of MTS in the visceral site we performed extensive ileal and mesentery resections since the latter had shortened and angulated the intestinal loops producing a mechanical occlusive crisis, (2 cases) fig 4,. in percutaneous transsexual drainage for biliary tract decompression followed by a resection of the biliary tract with anastomosis with roux loop (5 cases). In regional implant surgery of arterial or portal perfusion apparatuses (5 cases) in gastric cancer with lymph node diffusion (3 cases) and in pancreatic tumors with tumor body tail (3 cases) in which the criteria of radicality oncology were possible. In cases in which the search for the primary tumor was unsuccessful, ie in 30% (9 cases) of the patients, the surgical treatment was determined by an evaluation of the relationship between the general state of the patient and the clinical symptomatology, the histological characters extension. The patients who therefore remained without identification of the primary site were sent to the oncologist with cytological examinations that very often did not allow a definitive diagnosis. chemotherapy after research and histological confirmation of metastatic ca to occult site, provided a protocol with pharmacological associations such as: 5- fluoro uracil adriamycin mitomycin C, Cisplatin. Paclitaxel. thanks to the molecular study of the tumor the combined therapies have been proposed since the genetic characteristics of the primitive tumor are modified in the metastasis and therefore a therapy that matches the most suitable drugs to the various types of neoplasia has more chances of success. With these therapeutic protocols, positive results were obtained with regression of disease progression in 35-40% of cases. In this subgroup of patients the new cancer drugs were tested in order to obtain a greater number of positive responses. In addition to biological drugs, immunological drugs (bevacizumab) were associated with so-called immunomodulatory antibodies, which activate the patient's antitumor defenses by acting directly on targets that are no longer expressed by the tumor but by our own lymphocytes; the binding to these targets expressed by T lymphocytes activates them and "specializes them" in recognizing and subsequently effectively destroying cancer cells. the study is being processed, the results of which will be analyzed and discussed at the end of the therapeutic protocol

DISCUSSION

A problem that unfortunately still hinders the spread of drugs with a molecular target is also their high cost, their use on different tumors will and will have to contribute to reducing the costs in addition to the market competition between the various pharmaceutical companies that are developing these drugs. (6,7,8) In this study, we found that in the subgroup of patients given molecular targeted drugs (9 cases, 30%) we also obtained an improvement in overall quality of life, an aspect that is increasingly important. Diagnostic imaging has played a key role in TPOs with the identification of the anatomical site of the tumor lesion in which PET / CT and MRI were diagnostic tests for major images, as they showed a high sensitivity in the study and framing especially in those cases of TPO, which had a single metastatic site in which it is possible to program a curative therapy. Their sensitivity increased when the TPO had only lymph node, (6,10,11) with the identification of the primary site between 45% -55% of cases observed. the contribution of the immunohistochemical examination was also fundamental in terms of diagnostic accuracy. The analysis of the CK-7 and CK-20 low molecular weight cytokeratins, and their combination directed the diagnosis towards a specific tumor origin. studies (12,13,14) such as that AA aimed at identifying tissue of TPO origin have shown that the evaluation of the qRT-PCR based on the analysis of 92 genes has demonstrated an accuracy rate of 77% and is commercially available. With the evaluation of the gene expression profile an 88% sensitivity and a 99% specificity of diagnosis in a TPO are obtained. So although the literature data do not allow their full use on a large scale, however, we are convinced that in this pathology the evaluation of the gene profile is essential. In the patients with TPO, the initial work-up involving a complete evaluation of the clinical history, serological and accurate clinical examination, allowed to identify the primary site only in 25% of cases.(15,16,17) After completing the II level diagnostic procedure we performed, we obtained a percentage of definitive histological diagnosis and of an anatomical site of the primary lesion, which was 70%. (18,19.20)the cancer therapy that is very useful for these patients is still based on the oncologist's experience since there are no randomized clinical trials. surgical resection in association with palliative pharmacological protocols achieved median survival of 12.3 months.

CONCLUSIONS

TPOs require careful evaluation for each individual case. the current literature expresses conflicting opinions that tend to dissuade the prolonged treatment, even though it is evident that immunomodulatory drugs pose a cautious optimism in the treatment of neoplasm. the definition of the histological type of the tumor remains the fundamental moment of the therapeutic strategy and the immunohistochemistry in association with the tumor's genetic profile have been confirmed essential to the

achievement of the anatomopathological diagnosis, and furthermore the abundance of the biopsy material is not necessary. In relation to the tumor site, II-level diagnostic imaging (PET / CT and MRI) is able to locate the site of the primary tumor in 70% of cases. In late-onset forms that present with atypical thrombophlebitis, or in which the TPO site can not be identified, the spontaneous question is whether diagnostic in-depth analysis in terms of costs and benefits and of the achievable benefits is useful. On the possible causes for which the TPO can not be found, the hypothesis of the miniscule dimensions remains valid, or that the tumor has undergone spontaneous remission, the latter hypothesis of research on the different immunological phenotype, A last hypothesis remains the removal to followed by biopsies, currettages, electrocutions, of the primary lesion.

References

1. Hemmischi *et al* familiar risks in cancer of unknown primary tracking the primary sites J Clin.Oncol 2011 29,435-440
2. Chu PA *et al* keratin espression in human tessues and Neoplasms Histology 2011, 40 ,403.439.
3. Pavlidis N, Briasoulis E, Hainsworth J, Greco FA. Diagnostic and therapeutic management of cancer of an unknown primary. Eur J Cancer 2003; 39: 1990-2005
4. Dowell JE, Garrett AM, Shyr Y, Johnson DH, Hande KR. A randomized Phase II trial in patients with carcinoma of an unknown primary site. Cancer 2001; 91: 592-597
5. Paik S, Tang G, Shak S, Kim C, Baker J, Kim W, *et al*. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol. 2006;24(23):3726–34.
6. Tsoi DT, Inoue M, Kelly CM, Verma S, Pritchard KI. Cost-effectiveness analysis of recurrence score-guided treatment using a 21-gene assay in early breast cancer. Oncologist. 2010;15(5):457–65.
7. Mandrekar SJ, Sargent DJ. Predictive biomarker validation in practice: lessons from real trials. Clin Trials. 2010;7(5):567–73.
8. Sun X, Briel M, Walter SD, Guyatt GH. Is a subgroup effect believable? Updating criteria to evaluate the credibility of subgroup analyses. BMJ. 2010 340:c117.
9. Giorgio Maria Paul Graziano *et al* Early Epithelial Ovarian Carcinoma Treatment *International Journal of New Technology and Research* (IJNTR) ISSN:2454-4116, Volume-2, Issue-5, May 2016 Pages 69-74
10. Giorgio Maria Paolo Graziano *et al* Clinical and Molecular Anatomy of Gastrointestinal Stromal Tumors (GIST) International Journal of New Technology and Research (IJNTR) ISSN:2454-4116, Volume-2, Issue-4, April 2016 Pages 110-114
11. Giorgio Maria Paul Graziano1 *et al* Vascular Thoracic Fibrous Adipose Tissue (New Disease) J Pharm Biomed Sci | Vol. 06 No. 07 | 419–424
12. Giorgio Maria Paul Graziano " Which Treatment In Cystic Tumors of The Pancreas: Conservative or Resection *International Journal of Current Advanced Research Vol 5, Issue 8, pp 1190-1198, August 2016*
13. Giacomini M, Abelson J, Goldsmith L, Levin L, DeJean D, Smith A. Social values and health technology policy analysis: the role for qualitative social science and humanities research evidence. Canadian Agency for Drugs and Technology in Health (CADTH) Annual Symposium. Halifax, Nova Scotia 2010 Apr; 19.
14. Giorgio Maria Paolo Graziano *et al*.2017, Papillary Bladder Tumor. *Int J Recent Sci Res.* 8(7), pp. 18485-18490.DOI: http://dx.doi.org/10.24327/ijrsr.2017.0807.0518
15. Giorgio Maria Paolo Graziano *et al*.2017, Role of Genetic Mutations In The Diagnosis of Gallbladder Neoplasms. *Int J Recent Sci Res.* 8(10), pp. 20908-20913. DOI: http://dx.doi.org/10.24327/ijrsr.2017.0810.0982
16. Giorgio Maria Paolo Graziano *et al*.2017, Which Treatment In The Zenker Diverticulum. *Int J Recent Sci Res.* 8(11), pp. 21612-21616. DOI: http://dx.doi.org/10.24327/ijrsr.2017.0811.1107
17. Giorgio Maria Paolo Graziano *et al*.2017, The Antibiotic Is Needed In Clean Surgery?. *Int J Recent Sci Res.* 8(12), pp. 22339-22342. DOI: http://dx.doi.org/10.24327/ijrsr.2017.0812.1247
18. *Cavallaro A, Paolo Graziano GM, Cavallaro M, Graziano A (2015) The Neuroendocrine Cancer. Personal Comments and Operational Remarks. J Surg Surgical Res 1(3): 053-058. DOI: 10.17352/2454-2968.000014*
19. M, Iwata H, Yamanaka T, Masuda N, Ohno S, Nakamura S, *et al*. Clinical significance of the 21-gene signature (Oncotype DX) in hormone receptor-positive early stage primary breast cancer in the Japanese population. Cancer. 2010; 116(13):3112–8.
20. Dowsett M, Cuzick J, Wale C, Forbes J, Mallon EA, Salter J, *et al*. Prediction of risk of distant recurrence using the 21-gene recurrence score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: a TransATAC study. *J Clin Oncol*. 2010; 28(11):1829–34.

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