# Giant carcinosarcoma of the ovary. A case report and review of the literature

**Raul Josue Guerrero Caballero M.D.**
**Yamileth Lopez Plata M.D.**
**Adalberto Flores Coutiño M.D.**

***Mexico City, Mexico.***

Case Report

General Surgery

OPEN ACCESS

**BACKGROUND**. Carcinosarcoma is defined as a mixed malignant proliferation formed by two contingents, one epithelial, the other mesenchymal, also known as malignant mixed Müllerian tumor, is one of the rarest histologic subtypes of the ovary, accounting for 1 to 4% of all ovarian tumors. OCS (Ovarian carcinosarcoma) can be found in the genitourinary tract, the most common site being the uterus, followed by the ovary, fallopian tubes, cervix, vagina, peritoneum, breast and urethra. The rarity of the disease generates much controversy about the histogenesis, prognostic factors and treatment of OCS. OCS is usually found after menopause, with a median age of 65 years. Risk factors are the same as for ovarian carcinomas and sarcomas: obesity, nulliparity, exogenous estrogens, radiation therapy, and prolonged use of tamoxifen. The clinical presentation is usually abdominal pain, early satiety, gastrointestinal dysfunction, depending on the size, to the point of causing intestinal occlusion. The diagnosis of carcinosarcoma should be approached comprehensively. Symptoms, radiological findings and tumor marker levels should be taken into account. Almost all patients will express CA-125 antigen, at a value above 75 U/ml However, the final diagnosis can only be made after histopathological examination.
Cytoreductive surgery followed by chemotherapy with paclitaxel and/or platinum is considered the optimal and most effective treatment.

**KEY WORDS**: Ovary carcinosarcoma, ovary tumor.

## Introduction

Carcinosarcoma, also called mixed mesodermal tumor or mixed mullerian malignant tumor, is a pathological entity that combines a sarcomatous component with a carcinomatous component. Carcinosarcoma is defined according to the WHO 2008 classification by the mixed malignant proliferation formed by two contingents, one epithelial, the other mesenchymal.[1]

Ovarian cancer is the fifth most common cause of cancer death among women, and ninety percent of ovarian cancers are of an epithelial cell type, while sex cord stromal tumors and malignant ovarian germ cell tumors are relatively rare. Ovarian carcinosarcoma (OCS), also known as malignant mixed müllerian tumor, is one of the rarest histologic subtypes of the ovary, accounting for 1-4% of all ovarian tumors.[3]

Carcinosarcomas are often found after menopause at an average age of 60 to 70 years. More than two-thirds of patients with OCS are diagnosed at an advanced stage.4 It is an aggressive tumor with a dismal prognosis: median patient survival is less than two years.[3]

## Case report

A 46-year-old female patient with no history of chronic degenerative diseases, denies smoking and other drug addictions, refers exposure to biomass for 40 years, gynecological and obstetrical history, gestation 2 deliveries 2, denies use of contraceptives, or planning method. Surgical history of left oforectomy for mucinous ovarian cyst 5 years ago. She started 2 years ago with an increase in abdominal volume which she attributes to food intake, but 6 months ago she presented with asthenia, adynamia and dyspnea as well as changes in her defecatory habits, which progressed to intolerance to the oral route, abdominal pain and absence of bowel movements, so he was admitted to the medical unit where imaging studies were performed identifying giant tumor which conditions extrinsic compression of bowel loops, surgical management was decided finding a giant right adnexal tumor of 60x40cm weighing 11kg, was found, it was sent to transoperative study with a report of malignancy and cytoreductive surgery was performed.

*From the Department of General Surgery at Hospital Juarez de Mexico, Mexico City, Mexico. Received on September 2, 2021. Accepted on September 7, 2021. Published on September 9, 2021.*


DOI: 10.17605/OSF.IO/MEKCB

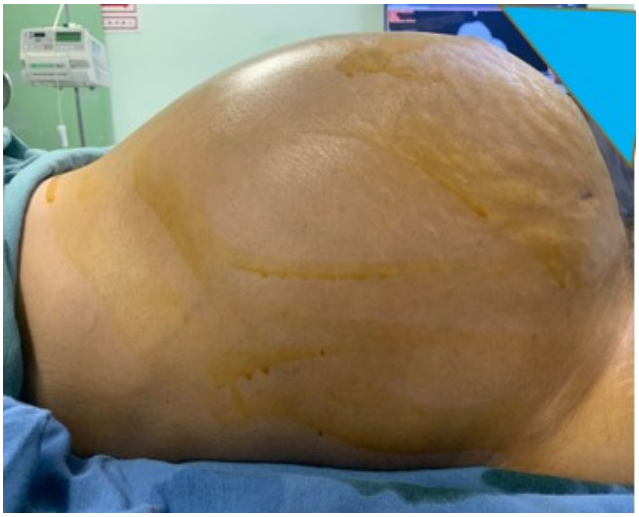

**Figure 1.** Abdomen with giant ovarian tumor lateral view.

The patient underwent cytoreductive surgery since tumor resection was performed, bilateral salpingo-oophorectomy plus hysterectomy with inguinal lymphadenectomy plus total omentectomy plus resection of peritoneal implants and diaphragmatic cupola, patient who evolved favorably in the postoperative period with start of oral diet 2 days postoperatively and was discharged 5 days after surgery, histopathological analysis was performed with a report of carcinosarcoma of the ovary, was sent to medical oncology for chemotherapy with carboplatin/paclitaxel, currently under follow-up 6 months after diagnosis, with moderate to severe ascites which has been performed paracentesis on 2 occasions, also presents right pleural effusion which has been performed thoracentesis on one occasion.

## Discussion

OCS can be found in the genitourinary tract, with the most common site being the uterus, followed by the ovary, fallopian tubes, cervix, vagina, peritoneum, breast and urethra.[3]

The rarity of the disease generates much controversy about the histogenesis, prognostic factors, and treatment of OCS.

These tumors are subclassified as "heterologous" (non-ovarian native tissue) or "homologous" (ovarian native tissue) according to the presence or absence of a component stroma containing mesenchymal tissue that is not normally found in the ovary.[2]

OCS are usually found after menopause, with a median age of 65 years. The risk factors are the same as for ovarian carcinomas and sarcomas: obesity, nulliparity, exogenous estrogens, radiation therapy, and prolonged use of tamoxifen.[2]

Patients usually have advanced disease at the time of diagnosis. Most patients are Caucasian and

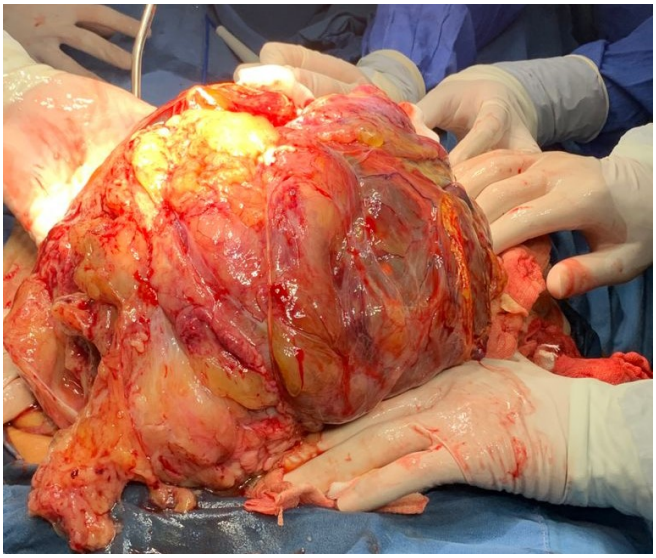

**Figure 2.** Irregular heterogeneous right adnexal tumor with adherent omentum.

have stage III-IV disease and spread beyond the ovary (> 90%) at diagnosis. MMMT has a worse survival rate than high-grade ovarian cancer at the same FIGO stage, with approximately 75% of reported patients dying from the disease within an average of 12 months postoperatively.[3]

The pattern of spread is similar to epithelial ovarian carcinoma, especially high-grade serous carcinoma (HGSC), with early serous and peritoneal spread, much earlier than HGSC.[2]

The macroscopic appearance is that of an easily large (5-10 cm), solid and/or cystic, grayish-brown tumor, often showing areas of necrosis and hemorrhage.[1]

Histologically, OCS contains both carcinomatous (malignant epithelial) and sarcomatous (mesenchymal) components. The carcinomatous component is usually serous, endometrioid, clear cell or undifferentiated adenocarcinoma. The sarcomatous component may consist of native ovarian homologous tissue or non-native ovarian etherologous tissue. Examples of ovarian homologous sarcomatous components include endometrial stromal sarcoma, fibrosarcoma, and leiomyosarcoma, while examples of heterologous sarcomatous components include chondrosarcoma, rhabdomyosarcoma, and, rarely, osteosarcoma or liposarcoma.[4]

## Pathogenesis

Three theories have been suggested to explain the histogenesis of gynecologic carcinosarcoma: biclonal (collision) and monoclonal (combination and conversion) theories.

The collision theory suggests that carcinoma and sarcoma are two independent tumors that originate from a separate cell, which then fuse. The combination


DOI: 10.17605/OSF.IO/MEKCB

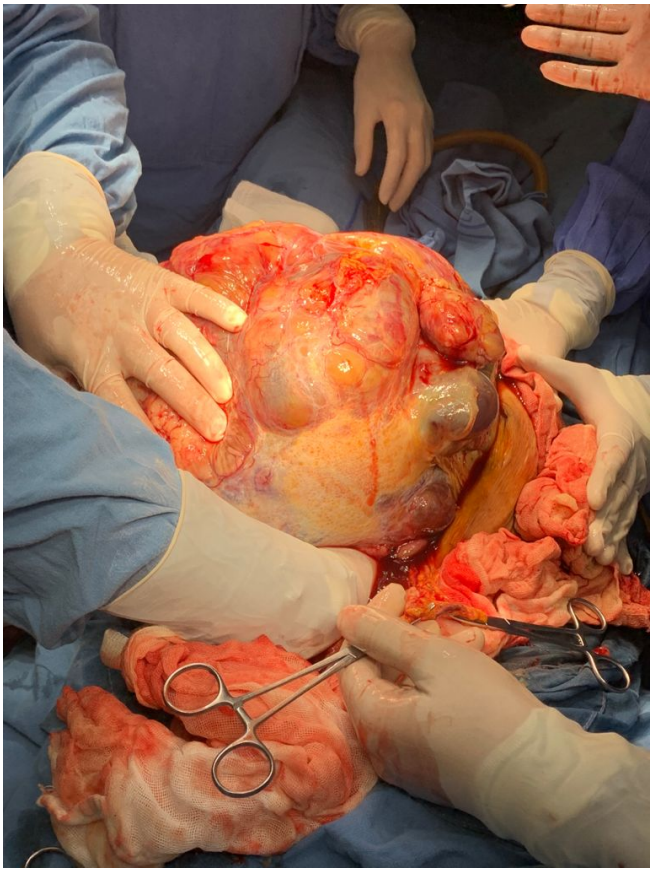

**Figure 3.** Excision of tumor

theory assumes that the sarcoma and carcinoma components are derived from a single stem cell and undergo divergent differentiation early in tumor evolution. Conversion theory states that an epithelial cell undergoes metaplasmic differentiation that initiates tumor genesis.[3]

Data on molecular genetic alterations, gene expression status and epigenetic profiles of OCS are scarce and the few published studies are based on a small number of tumors. Mutations of the tumor protein gene (TP53) are assumed to be the most frequent alteration, observed in 50% of the tumors analyzed. Other mutations, reported with lower frequencies, affect the hospatidylinositol4,5-bisphosphate 3-kinase catalytic subunit alpha gene (PI3K3CA), the rat sarcoma ki-ras2 kirsten viral oncogene homolog (KRAS), the catenin beta 1 gene (CTNNB1) and the euroblastoma virus RAS (V-Ras) oncogene homolog (NRAS).[5]

## Prognostic factors

In terms of histopathologic prognostic factors, the significance of the presence or absence of a heterologous mesenchymal component is unclear. Some studies have reported that the presence of sarcomatous heterologous elements is associated with a poor prognosis, whereas others presented that the heterologous component does not affect survival.

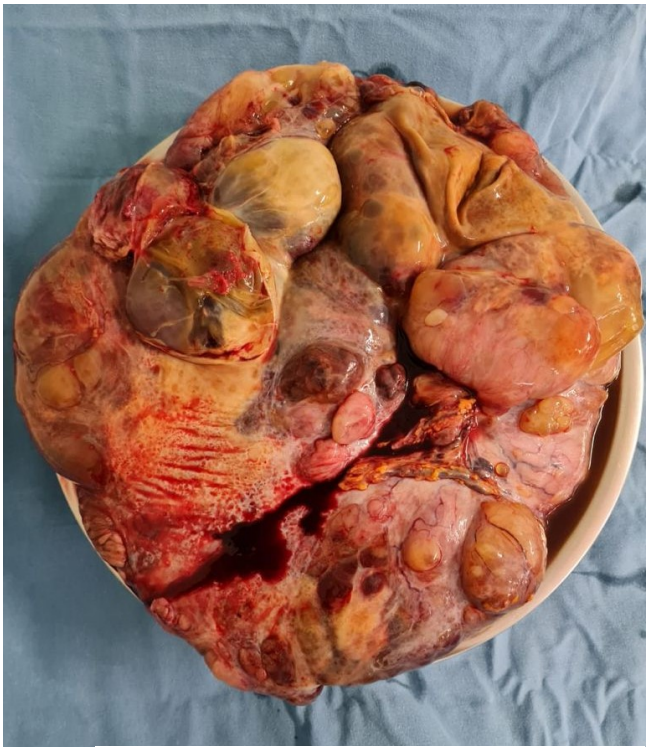

**Figure 4.** Carcinosarcoma of right ovary. Macroscopic appearance.

However, the histologic feature of the epithelial element may predict outcome.[6]

Metastatic disease may be related to the extent and vascular invasion of the myometrium. The presence of a sarcomatous component greater than 25%, as well as a high number of small vessels in the primary tumor, have also been associated with worse survival; moreover, tumors with serous epithelial components negatively affected survival compared with nonserous components. In a study of 25 patients with uterine OCS, increased expression of VEGF, VEGFR-3 and number of vessels correlated with poor survival.[6]

OCS have been reported to overexpress p53 in a relatively higher proportion compared to other gynecological cancers, this was associated with advanced stage and worse survival. Corresponding overexpression of P53 has been found in approximately 10-15% of early cases and in 40-50% of advanced ovarian and endometrial adenocarcinomas.[6]

To date no study has been able to demonstrate that stage is a prognostic factor, the rarity of early stage cases reduces the statistical power in reported case series. Hellstrom et al, found that stage I or II patients had better survival than those with stage III or IV disease however George et al. showed that stage II and more advanced stage disease had poor overall survival.[6]

A study designed to evaluate PD-L1 and intratumoral CD8+ T-cell expression by immunohistochemistry demonstrated a prognostic


DOI: 10.17605/OSF.IO/MEKCB

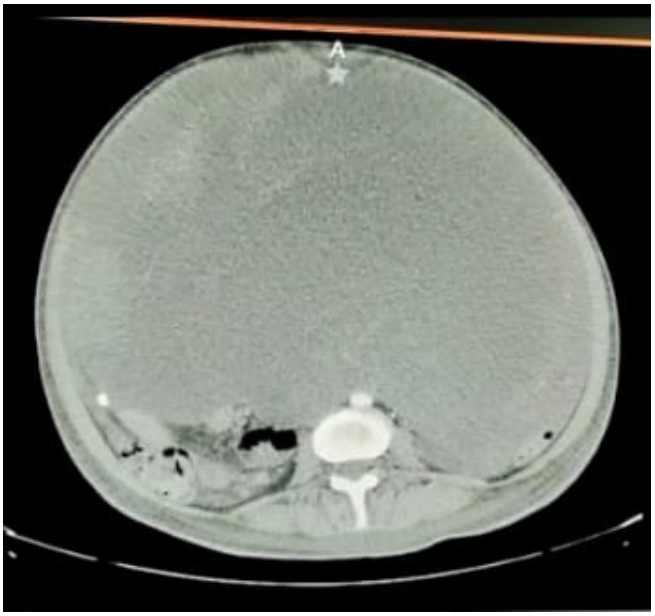

**Figure 3.** Abdominal CT scan with heterogeneous adnexal mass.

value of CD8+ T-cells and PD-L1 expression. These results suggest that, tumor CD8 + T lymphocytes and PD-L1-negative mesenchymal PD-L1 expression appear to be associated with improved survival in OCS.[6]

## Clinical presentation

The clinical presentation usually resembles that of ovarian adenocarcinoma. However, it appears that the age at diagnosis is somewhat older, with a median age at diagnosis at diagnosis of 60-70 years. Symptoms include abdominal pain, early satiety, gastrointestinal dysfunction, depending on the size, which can become large and cause intestinal occlusion with oral intolerance, nausea and vomiting, and even dyspnea and pleural effusion. Ascites is also found, more in advanced stages. Hepatic or pulmonary metastases are rarely present, unlike in uterine locations.[1]

On initial examination a palpable mass may be appreciated, it is estimated that more than 90% of women will have disease beyond the ovary, with one third of cases involving both ovaries and ascites. Several authors have reported lymph node metastases in more than one-third of cases, lymph nodes in more than half of the patients at the time of initial diagnosis.[7]

The diagnosis of carcinosarcoma must be approached comprehensively. Symptoms, radiological findings and tumor marker levels should be taken into account.[10] Almost all patients will express CA-125 antigen, at a value above 75 U/ml (Sood et al., 1998). This could be useful in assessing response to treatment (Brown et al., 2004). Both epithelial and sarcoma elements are present in metastatic disease.[7]

However, the final diagnosis can only be made after histopathological examination of material taken during surgery. Immunohistochemistry can also be used in the diagnosis. Due to the diversity of the histopathologic structure of the described neoplasm, no characteristic immunohistochemical pattern has been found among the cases analyzed. However, some cases are found to be positive for epithelial membrane antigen (EMA), cytokeratin and vimentin.[10]

Ovarian carcinosarcomas are not usually implicated in hereditary cancer syndromes. Carnevali et al. described two cases of carcinosarcoma that occurred in women with hereditary cancer syndromes. One case in a woman with a mutation in the BRCA1 gene, the other in a woman with Lynch syndrome. These two cases demonstrate that, if carcinosarcoma occurs at a young age and there is a family history of multiple cancers, an inherited cancer susceptibility syndrome may be suspected.[12]

## Treatment

Because carcinosarcoma is such a rare tumor, no clear guidelines have yet emerged on how to treat it. Cytoreductive surgery followed by chemotherapy with paclitaxel and/or platinum is considered the optimal and most effective treatment for OSC. Maximal cytoreduction in patients with advanced stage carcinoma has been shown to have benefits and improve prognosis and total cytoreduction should be the goal of all surgery.[10]

Considering the low incidence of these tumors, prospective trials of chemotherapy have been difficult to perform. Thus, the preferred first-line chemotherapy for patients with ovarian carcinosarcoma remains unknown.8 However, the data guiding chemotherapy for the treatment of ovarian carcinosarcoma are largely extrapolated from studies on the treatment of uterine carcinosarcoma. Historically, ovarian carcinosarcomas have often been treated with the same first-line chemotherapy as uterine carcinosarcomas, ifosfamide/paclitaxel. In addition, multiple phase II studies investigating the use of carboplatin/paclitaxel in uterine carcinosarcoma demonstrated efficacy with this regimen.[9]

Small case series have reported on the efficacy of these and other regimens in the treatment of ovarian carcinosarcoma.

Results from NRG Oncology's phase III clinical trial comparing paclitaxel plus carboplatin with paclitaxel plus ifosfamide in women with recurrent stage I-IV carcinosarcoma of the uterus or ovary show, among other things, that treatment with paclitaxel plus carboplatin is associated with longer progression-free survival than treatment with paxlitaxel plus ifosfamide.[10] In a cohort of 31 patients


DOI: 10.17605/OSF.IO/MEKCB

with ovarian carcinosarcoma Brackmann et al. performed the comparison of patients treated with carboplatin/paclitaxel compared to ifosfamide/paclitaxel demonstrating that overall survival was similar in all treatment groups. However, patients treated with carboplatin/paclitaxel had statistically significantly longer progression-free survival compared to those receiving ifosfamide/paclitaxel (17.8 vs. 8.0 months, p = 0.025).[11]

Given the rarity and aggressive nature of this tumor further studies on optimal first-line chemotherapy are warranted.

Due to the small size of the patient groups analyzed it is difficult to determine whether surgery alone or surgery followed by chemotherapy have better survival Among the articles reviewed, Patnayak et al. in a 2015 article mention the search for new treatments for carcinosarcoma. They describe the potential use of the humanized anti-Trop-2 antibody in patients with refractory carcinosarcomas overexpressing Trop-2. They also mention that human epidermal growth factor-2/neu may be a new target for immunotherapy. [10]

## Conclusion

Ovarian carcinosarcoma is a rare tumor with a poor prognosis by itself due to its histology, which makes it highly aggressive. However, due to its low incidence and rapid progression to death, its adequate management has not been defined, so surgery continues to be the most adequate management of this type of tumor accompanied by adjuvant chemotherapy.

The clinical presentation of ovarian carcinosarcoma usually resembles that of adenocarcinoma. However, it appears that the age at diagnosis is somewhat older, with a mean age at diagnosis at the time of diagnosis of 60-70 years; however, this does not correlate with our clinical case, so it is of great importance to report this type of disease, as the statistics may change according to future reports.

## Conflicts of interests

There was no conflict of interest during the study, and it was not funded by any organization.

## References


1. Guy J-B, Trone J-C, Casteillo F, Forest F, Pacaut C, Moncharmont C, et al. Carcinosarcomes gynécologiques : revue générale et principes de prise en charge. Bull Cancer. 2014;101(7–8):760–4.
2. Saida, T., Mori, K., Tanaka, Y.O. *et al.* Carcinosarcoma of the ovary: MR and clinical findings compared with high-grade serous carcinoma. *Jpn J Radiol* 39, 357–366 (2021).
3. Kostov S, Kornovski Y, Ivanova Y, Dzhenkov D, Stoyanov G, Stoilov S, et al. Ovarian carcinosarcoma with retroperitoneal para-aortic lymph node dissemination followed by an unusual postoperative complication: A case report with a brief literature review. Diagnostics (Basel). 2020;10(12):1073.
4. Daimon A, Fujiwara S, Tanaka Y, Tanaka T, Ohmichi M. A rare case of ovarian carcinosarcoma with squamous cell carcinoma. J Ovarian Res. diciembre de 2019;12(1):32.
5. Brunetti M, Agostini A, Staurseth J, Davidson B, Heim S, Micci F. Molecular characterization of carcinosarcomas arising in the uterus and ovaries. Oncotarget. 4 de junio de 2019;10(38):3614-24.
6. Stergios Boussiosa,f,∗ , Afroditi Karathanasia , Nikolaos Zakynthinakis-Kyriakoub , Alexandros K. Tsiourisc , Aikaterini A. Chatziantonioud , Foivos S. Kanellosc , Konstantina Tatsi Ovarian carcinosarcoma: Current developments and future perspectives.
7. del Carmen MG, Birrer M, Schorge JO. Carcinosarcoma of the ovary: A review of the literature. Gynecologic Oncology. abril de 2012;125(1):271-7.
8. Mano MS, Rosa DD, Azambuja E, Ismael G, Braga S, D'Hondt V, Piccart M, Awada A. Current management of ovarian carcinosarcoma. Int J Gynecol Cancer. 2007;17(2):316–24.
9. Homesley HD, Filiaci V, Markman M, Bitterman P, Eaton L, Kilgore LC, Monk BJ, Ueland FR, Gynecologic Oncology G. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma: a gynecologic oncology group study. J Clin Oncol. 2007;25(5):526–31
10. Kozłowski M, Nowak K, Kordek A, Cymbaluk-Płoska A. Therapeutic Management of Rare Primary Ovarian Neoplasms: Carcinosarcoma, Leiomyosarcoma, Melanoma and Carcinoid. IJERPH. 23 de julio de 2021;18(15):7819.
11. Brackmann M, Stasenko M, Uppal S, Erba J, Reynolds RK, McLean K. Comparison of first-line chemotherapy regimens for ovarian carcinosarcoma: a single institution case series and review of the literature. BMC Cancer. diciembre de 2018;18(1):172.
12. Carnevali IW, Cimetti L, Sahnane N, Libera L, Cavallero A, Formenti G, Riva C, Tibiletti MG. Two Cases of Carcinosarcomas of the Ovary Involved in Hereditary Cancer Syndromes. Int. J. Gynecol. Pathol. 2017, 36, 64–70.


Raul Josue Guerrero Caballero
Department of General Surgery
Hospital Juarez de Mexico
Mexico City, Mexico
josue_guerrero_21@hotmail.com

 DOI: 10.17605/OSF.IO/MEKCB