

## LETTERS TO THE EDITOR

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### Contribution disclosures

Dear Editor,

When a journal publishes research article, the authorship of one author is clear. However, when the number of authors of the article increases, the contribution of each author is more complex and his position on byline does not give proper information [1,2]. The trend toward increasingly collaborative research, the team science, has many advantages, but it also faces potential problems, including the size of optimal group of authors, their participation in the study and interpretation of the results obtained. Appropriate recognition to individual members of the science team in the scientific report should be clear [3]. Therefore, many journals, e.g., *Science*, *JAMA*, *PNAS*, *BMJ*, and *Annals of Internal Medicine*, require that each coauthor disclose his contribution. Generally, journals do not limit the number of authors if the authors accepted the authorship criteria of the journal.

In the *JBUON* [4], there is a following statement for fifteen authors: "The authors contributed equally to this work." A reader could immediately notice that such statement is insufficient.

My suggestion is following. The editorial board of the *JBUON* should consider introducing a contributor-ship policy for each author in the original article, short communication, special article, and review article. This measure will give to the authors not only the proper credit and responsibility, but it will also be the way to eliminate non-author contributors [5,6].

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### Topically applied vasoconstrictor while decreasing radiation dermatitis may increase local recurrences in post-lumpectomy breast cancer patients who received radiotherapy

Dear Editor,

Radiodermatitis is the primary treatment-limiting acute side effect of adjuvant breast radiation and may cause treatment breaks and delays that have an adverse impact on tumor recurrence. Topical agents that have been evaluated include Aloe vera, Biafine, and steroidal and nonsteroidal anti-inflammatory agents. However, none has been shown to be clinically effective. Furthermore, Cleary and colleagues reported on a phase IIa study of topically applied NG12-1 vasoconstrictor to prevent radiodermatitis

in post-lumpectomy breast cancer patients who received at least 40 Gy to the whole breast using standard regimens [1]. They found that this agent significantly suppressed radiation dermatitis in breast cancer patients. However, there is a concern about the sequelae of vasoconstriction by using topically applied NG12-1 vasoconstrictor which may lead to temporary hypoxia in the breast tissue. Then, breast tumor cells in turn may be resistant to radiotherapy in this hypoxic microenvironment [2]. As a consequence, we might expect to see more local recurrences. This issue merits further investigation.

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## Primary gastric choriocarcinoma

Dear Editor,

Choriocarcinoma occurs commonly in females as a gestational malignant neoplasia. It rarely has a non-gestational origin, when it is found in the retroperitoneum, the mediastinum, or intracranially. Primary gastric choriocarcinoma (PGC) is a rare tumor constituting less than 1% of all gastric cancers [1]. Thirty percent of PGC are at a metastatic stage at diagnosis [2] and the prognosis is usually poor.

A 73-year-old man was admitted to the surgery department with dyspeptic complaints. Abdominal CT scan revealed gastric wall thickening (14mm) in the small curvature, and enlarged paraaortic lymph nodes. Esophagogastroduodenoscopy demonstrated an ulcerated lesion on the lesser curvature and biopsy revealed a gastric adenocarcinoma. The patient was subjected to total gastrectomy and the pathologic examination revealed an ulcerated solid lesion on the small curvature that extended to the serosa, peritoneum and liver surface, which also had lymphovascular invasion, while metastasis was detected in 6 out of 20 lymph nodes removed. This lesion contained two components, one of which was adenocarcinoma and the other one was composed of multinucleated giant cells. There was a typical plexiform dimorphic pattern of syncytiotrophoblasts under microscopic examination and immunohistochemical (IHC) analysis showed positivity for  $\beta$ -human chorionic gonadotropin ( $\beta$ -HCG). These findings were consistent with PGC. PET scan showed no evidence of any involvement in the bone, liver or lung. The patient's CEA and  $\beta$ -HCG values were 3 ng/ml (range 0-3) and 4.06 ng/ml (range 0-2), respectively. Other tumor markers and AFP were negative. The patient received 4 cycles of EP adjuvant chemotherapy (etoposide 100 mg/m<sup>2</sup> on day 1, and cisplatin 20 mg/m<sup>2</sup> on days 1-5) and has now been monitored for 10 months without recurrence.

Choriocarcinomatous differentiation has been specified in tumors arising from many organs, such as bladder, lung, rectum, colon and stomach. PGC is a rare and aggressive tumor with early metastasis. It also commonly secretes high levels of  $\beta$ -HCG. The diagnosis of PGC depends on the choriocarcinoma component in the pathological specimen and presence of  $\beta$ -HCG positivity on IHC analysis. Also, elevation of serum  $\beta$ -HCG without other site displaying tumor mass are necessary. PGC and adenocarcinoma are often found together, similar to our case, where it was primarily identified as adenocarcinoma by endoscopic biopsy. Pure PGC is very rare. The pathogenesis of PGC is still uncertain. Some theories on the histopathogenesis of PGC

propose a long delayed metastasis from a genital primary lesion, arising from gastric teratoma, and retro-differentiation of gastric carcinoma cells to embryonal ectodermal status with the ability to form trophoblasts [3]. Hepatoid adenocarcinoma can be considered in the differential diagnosis of PGC. Owing to lack of AFP increase in the plasma and absence of AFP or hepatocyte specific antigen in the pathological specimen this can be ruled out. Gastrectomy with lymph node dissection followed by chemotherapy is the treatment of choice for PGC. A standard treatment of PGC has not been established owing to the infrequency of this tumor. Some studies reported benefit of chemotherapy, such as FOLFIRI, EMA-CO (etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine), BEP (bleomycin, etoposide, cisplatin), and EP (etoposide, cisplatin) [4,5]. Our patient received EP chemotherapy to our patient and he is being monitored without disease relapse.

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## Outcome of breast cancer patients with mental disorders; we still need to learn more!

Dear Editor,

Information about the survival of patients with breast cancer with preexisting mental illness is limited, and elderly women are of special interest because they experience the highest incidence of breast cancer. Shinden and colleagues in their article [1] evaluated the clinical features of 46 patients with breast cancer and pre-existing mental disorders such as schizophrenia, dementia, and intellectual disability and compared them with a control group of 727 breast cancer patients without mental disorders seen during the same period. The authors noted that the biological characteristics of patients with mental disorders were similar to the control group. Eventually, they reported that patients with mental disorders receive less postoperative adjuvant chemotherapy; however, their outcomes were not worse than those of patients without mental disorders. Iglay et al. [2] compared all-cause and breast cancer-specific mortality for elderly patients with breast cancer with and without mental illness. Contrary to the study by Shinden et al. [1], they found a 20% increase in breast cancer-specific mortality hazard. They also observed that patients with severe mental illness were more likely to be diagnosed with advanced breast cancer with aggressive tumor characteristics [2]. Another study investigated diagnosis and treatment delays in elderly breast cancer patients with and without pre-existing mental illness [3]. They reported that patients with any mental illness experienced an increased risk for adjuvant chemotherapy

delay of  $\geq 90$  days from last operation (RR 1.13; 95% CI 1.01, 1.26) [3]. Taken all together, survival data in breast cancer patients with mental disorders are still questionable and warrant further investigation. Treatment delays in this specific population should also be taken into consideration for interpretation of survival outcome.

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## HPV mRNA expression profiling in head and neck squamous cell carcinomas

Dear Editor,

Human papillomavirus (HPV) involvement in head and neck squamous cell carcinomas (HNSCC) rises and progression represents a classical example of viral-mediated carcinogenesis. These SCCs demonstrate differences regarding sexual, molecular, epidemiological, and prognostic features compared to alcohol and tobacco depended ones [1, 2]. In fact, the incidence of smoking-associated HNSCC has declined, while HPV-associated HNSCC is on the rise. Similarly to cervical HPV-dependent infection, high risk (HR) HPV subtypes penetrate initially the cell membrane of the target cells as a simple (episomal) viral infection followed by HPV-DNA integration into the host cell genome leading to an aberrant oncogene E6/E7 expression. Inactivation of p53 and Rb suppressor genes are the main genetic abnormalities correlated with HPV E6/E7 increased production, respectively. Interestingly, new biomarkers, such as miRNAs expression have also been implemented in analyzing HPV-positive and HPV-negative HNSCC tumor tissues [3]. Concerning the methodology in confirming or not HPV presence in HNSCCs, implementation of HPV DNA and mRNA testing remain the main molecular approaches.

HPV DNA genotyping determines the episomal infection of the corresponding target cells mediated by specific HPV types. Polymerase chain reaction (PCR) combined with microarray technology has been used for HPV detection, genotyping, and viral load determination. In contrast to HPV DNA analysis, mRNA testing recognizes the malignant transformation of the host cell genome by measuring E6/E7 oncogene expression. Recently published studies have shown that E6/E7 mRNA detection not only in tissue specimens but also in serum could be a reliable method for monitoring the corresponding patients with oral squamous cell carcinomas (OSCCs). Based on their clinico-molecular data, HPV 16 E6/E7 mRNA expression not only served as a molecular marker of HPV infection but also acted as an independent risk factor for local recurrence (LR) [4]. They demonstrated that increased concentrations of serum anti-E7 antibodies were a marker of risk for LR in OSCC. Additionally, another study group co-analyzing HPV E6/E7 DNA, mRNA, and p16 (INK4a) in a series of HNSCC salivary oral rinses concluded that the detection of HPV-16 DNA in salivary oral rinse is indicative of HPV status in HNSCC patients and can potentially be used as a diagnostic tool [5]. Comparing p16 and E6/E7 mRNA as reliable mark-

ers for evaluating the progress of HPV-mediated HNSCC, those studies suggest that not the immunohistochemical pattern but the molecular profile provides better biological information.

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# Why babies do not want to nurse the premalignant breast side in breast-feeding mother? A possible sign of early diagnosis of breast cancer in younger women

Dear Editor,

In breast cancer some screening tests are used because they have been shown to be helpful both in early detection of cancer diagnosis and because they decrease the chances of dying of disease. Mammography is the most common screening test for breast cancer. Women aged 40 to 74 years who have undergone screening mammograms have a lower chance of dying from breast cancer than those who haven't [1]. However, younger women (less than 40 years of age) may be diagnosed with breast cancer anyway. The main reason for that is the lack of screening methods recommended for those younger women unless they had familial breast-ovarian cancer history at earlier age. Therefore, additional hints are needed to catch breast cancer as early as possible even at the premalignant phase in younger women [2]. It is well-known that breastfeeding, particularly a longer duration of breastfeeding, was inversely associated with higher risk of breast cancer [3]. Some anecdotal case reports were related with younger breast cancer patients; their detailed reproductive history indicated that the babies of younger breast cancer cases did not want to approach their mothers for sucking their breast, among them 1-3 years later after the breastfeeding stops. In the current literature, there were no data about this issue. Our hypothesis is that during breastfeeding period, a premalignant lesion located on the right or left breast which is called "intraductal region" may change the quantity or quality of breast milk produced from breast lobules. This abnormal breast milk might be disliked by the baby and this may result these babies to prefer the milk of the other breast. In support of this hypothesis, a recent study performed proteomics analysis of human breast milk to assess breast cancer risk [4] and the authors

reported that, despite a wide range in the time between breastfeeding and breast cancer diagnosis (cancer diagnosis occurred from 1 month before to 24 months after breastfeeding, the levels of some proteins differed significantly between cancer and control groups. These pilot data are supportive of the idea that molecular analysis of breast milk will identify proteins informative for early detection and accurate assessment of breast cancer risk. This hypothesis merits further investigation.

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