the diagnosis of leiomyosarcoma died for multiple peritoneal recurrences and lung metastases. The other two patients are still alive after 6 month of follow-up and show no local recurrences or metastases.

Discussion. Ulipristal acetate is a selective progesterone receptor modulator that has recently been approved for intermittent, long term, and preoperative treatment of moderate-to-severe symptoms associated with ULM in adult women of reproductive age. The reversible blocking of the progesterone receptor induced by UPA explains its anti-proliferative, anti-fibrotic and pro-apoptotic effects which are responsible of the reduction of ULM size. Moreover, due to its interaction with endometrial progesterone receptors, UPA induces amenorrhea reducing thus the severe bleeding related to ULM. Moreover, a considerable small percentage of patients (4.8%) has been reported to not benefit from UPA treatment and the possible motivations for this inefficacy are still debated. In this regard, a recent study identified the following predictive parameters of UPA treatment failure: young age (<35 ys), absence of previous pregnancy and the size of the dominant fibroid ≥ 80 mm. Hence, the persistence of heavy bleeding and pelvic pain during UPA treatment is not to be considered specific for the diagnosis of LMS, but the suspect of an unexpected LMS must be taken into consideration as a cause of inefficacy of this hormonal therapy. Similarly, our reported LMS cases were preoperatively misdiagnosed as benign smooth muscle tumors (ULM). Therefore, the treatment with UPA revealed to be ineffective or only partially beneficial, so that both patients experienced a rapid increase of symptomatology. To the best of our knowledge, a total of 6 cases of LMS treated with UPA for suspected ULM have been reported in the literature.

Conclusions. Our reported cases emphasize that the poor or absent response to Ulipristal Acetate treatment in addition to the instrumental evidence of a single mass may be indicative of the presence of an unsuspected leiomyosarcoma clinically and radiologically misdiagnosed as leiomyoma. The awareness of this possibility would avoid a delay in the diagnosis as well as unuseful and potentially dangerous treatments such as morcellation.

References

Gurusamy KS, Vaughan J, Fraser IS, et al. Medical therapies for uterine fibroids - a systematic review and network meta-analysis of randomised controlled trials. PLoS One 2016;26:11:e0149631.

Istre O. Unexpected uterine leiomyosarcoma during laparoscopic hysterectomy treated 6 months with ulipristal acetate and contained power morcellation. J Minim Invasive Gynecol 2017;24:198.

Biglia N, Carinelli S, Maiorana A, et al. Ulipristal acetate: a novel pharmacological approach for the treatment of uterine fibroids. Drug Des Devel Ther 2014;8:285-92.

MULTIVARIATE ANALYSIS OF HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL PROGNOSTIC FACTORS IN ENDOMETRIAL CARCINOMA

M. Paudice[1], L. Peñuela[2], C.M. Biatta[1], G. Scaglione[1], L. Valle[1], B. Spina[3], S. Ferrero[4], V.G. Vellone[1 5]

[1] Anatomia Patologica, DISC, Università di Genova; [2] UOSD Patologia Feto-perinatale, IRCCS Istituto Giannina Gaslini, Genova; [3] UO Anatomia Patologica, IRCCS Ospedale Policlinico San Martino, Genova; [4] Ostetricia e Ginecologia, DiNOGMI, Università di Genova; [5] UO Anatomia Patologica Universitaria, IRCCS Ospedale Policlinico San Martino, Genova

Objective. Endometrial carcinoma (EC) is the most common malignant disease of the female genital tract. It is the fifth cancer in women and the seventh cause of cancer death in North Europe. We investigated the prognostic role of some histopathological and immunohistochemical factors in EC in term of disease free survival (DFS) and overall survival (OS).

Method. Out of the total number of patients who had surgery for EC (S. Martino Polyclinic Hospital, Genoa, Italy) over the period 1.1.2013-1.7.2016, we considered only those with available clinical and radiological follow-up data after hysterectomy. Patients treated with neoadjuvant therapy were ruled out. All surgical specimens have been routinely processed to obtain 3-µm thick histological sections, finally stained with Hematoxylin and Eosin. As histopathological features, we considered histotype, stage at diagnosis, type of infiltration (infiltrative/expansive), desmoplasia (presence/absence), intratumoral necrosis (presence/absence), Tumor Infiltrating Lymphocytes (TIL; absent/mild or moderate/severe), lymphatic and blood vessels invasion (presence/absence). For each case the percentage of staining (%) of a panel of immunohistochemistry markers (IHC) including ERα, PR, Ki67, p53, β-catenin, E-cadherin, BCL-2 and Cyclin D1 has been investigated. Clinical, pathological and IHC data were entered in a Microsoft Excel© spreadsheet. Discrete and continuous variables were compared respectively using the $\chi 2$ test and Kruskal-Wallis test. Survival univariate analysis was studied with Kaplan- Meier survival curves, while survival multivariate analysis with Cox-Models. The significance was confirmed with the Log Rank Test. For statistical computation MedCalc© and OriginPro® programs were used.

Results. Out of 99 cases eligible for our purposes, we found 69 low-grade endometrioid (LGEC), 8 high-grade endometrioid (HGEC) and 22 other high-grade endometrial carcinomas (OHEC); the latter consisted of 6 serous, 4 carcinosarcoma, 2 clear cell, 8 mixed and 2 undifferentiated histotypes. The DFS multivariate analysis showed a strong positive correlation between poor prognosis and advanced stage (p=0.0042). The OS multivariate analysis revealed a positive correlation between poor prognosis and advanced stage (p=0.0003), presence of desmoplasia (p=0.04) and high Ki67 proliferative index (of borderline significant, p=0,052). Other factors - that resulted significantly correlated with the prognosis in univariate analysis - lost their role after the multivariate analysis. In univariate analysis, OHEC histotype was positively correlated with a worse prognosis when compared to endometriod type (OS: p=0.005; DFS: p=0.002). In the same way the low expression of PR was positively correlated with a poor prognosis (OS: p=0.017; DFS: p=0.014). Basically, some of the proposed prognostic factors seem just to well correlate with the stage of disease but they lose their independence in multivariate analysis.

Conclusions. In our small but representative case study, the prevalence of different EC histotypes are in line with the scientific Literature. The multivariate analysis confirmed the central role of the disease staging as the main important prognostic factor in EC both in term of OS and DFS. Moreover the presence of desmoplasia and the Ki67 proliferative index have demonstrated to be significantly correlated with OS.