Ganglioglioma arising in an ovarian teratoma

Angela Santoro ,[1] Nicoletta D'Alessandris,[1] Giulia Scaglione,[1] Gian Franco Zannoni [1,2]

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[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy
[2]Pathology, Catholic University, Rome, Italy

Correspondence to
Dr Gian Franco Zannoni, Pathology, Catholic University, Rome, 00168, Italy; gianfranco.zannoni@unicatt.it

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A pregnant 23-year-old woman presented during a gynecological ultrasound check-up with a 120×56×82 mm multilocular, non-echogenic, solid cystic left ovarian mass with a 12×33 mm internal papillary structure (Figure 1). High serum CA19.9 values were found (83 U/mL). CA125, carcinoembryonic antigen, and HE4 serum levels were within normal ranges. Evidence that the patient harbored a germline BRCA1 mutation (c.5266dupC–p.Gln1756Profs*74) prompted removal of the lesion after the pregnancy by a laparoscopic procedure with peritoneal/omental biopsies and peritoneal washing.

Pathologically, the lesion consisted of heterogeneous tissues: epithelia, cartilage, mature bone tissue, and mature disorganized nervous tissue (Figure 2A). More cellular areas were composed of a proliferation of astrocytic elements with abundant dense eosinophilic cytoplasm (Figure 2B–C), being immunohistochemically positive for glial fibrillary acidic protein (GFAP) (Figure 2E), vimentin and S100. A second cell population showed dysplastic neuronal morphology (Figure 2D) and immunoreactivity for synaptophysin, chromogranin A, and neurofilament protein (Figure 2F). The pathological findings were consistent with a mature cystic teratoma associated with a ganglioglioma. Because BRAFV600E is one of the described mutations in gangliogliomas,[1] BRAFV600E immunostaining was performed and was negative.

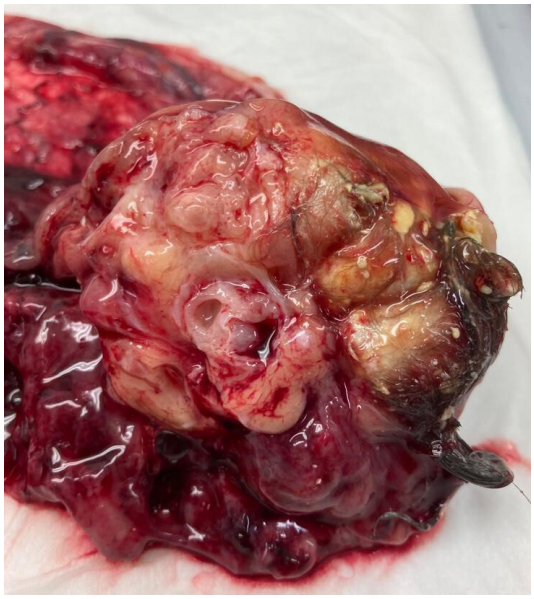

Figure 1 Macroscopic features. A 120×56×82 mm multilocular, non-echogenic, solid cystic ovarian mass in a pregnant woman.

DISCUSSION

The current 2021 World Health Organization (WHO) classification of central nervous system (CNS) tumors defines ganglioglioma as a glioneuronal neoplasm composed of well-differentiated dysplastic ganglion cells combined with neoplastic glial cells. In about 10–60% of cases, gangliogliomas harbor BRAFV600E mutations.[1] The prognosis is generally favorable (event-free survival 97% at 7.5 years). Therefore, gangliogliomas correspond to a CNS WHO grade I. Anaplastic gangliogliomas corresponding to gangliogliomas with an anaplastic glial component (conspicuous mitotic activity, high Ki67, necrosis, and microvascular proliferation) have been reported in 1–8% of cases with aggressive clinical behavior and a worse prognosis (recurrence in 50% of patients and median overall survival ranging from 25 to 44 months) (see Online Supplemental File 1). Due to the lack of in-depth molecular analyses in the different studies, the exact diagnostic criteria for this entity must be defined in further investigations.[1]

According to the WHO classification of female genital tumors, the occurrence of neuroectodermal neoplasm in ovarian teratomas is considered to be rare[2] and associated with the autoimmune N-methyl-D-aspartate receptor encephalitis.[3] However, our patient did not have neurological or psychiatric symptoms in her clinical history.

The occurrence of ganglioglioma in a teratoma has only been described in a single case report,[4] which was only published in abstract form and lacked images and a thorough clinical case discussion.

To date, CNS gangliogliomas have been reported in the setting of NF1 germline mutations but not BRCA mutations.[5] We describe the first extra-CNS ganglioglioma within an ovarian teratoma in a BRCA1 mutated patient. It is not clear whether the presence of BRCA1 germline mutation can play a role in the neoplastic transformation of ovarian teratomas and their biological behavior. Some authors have proposed possible etiopathogenetic mechanisms such as

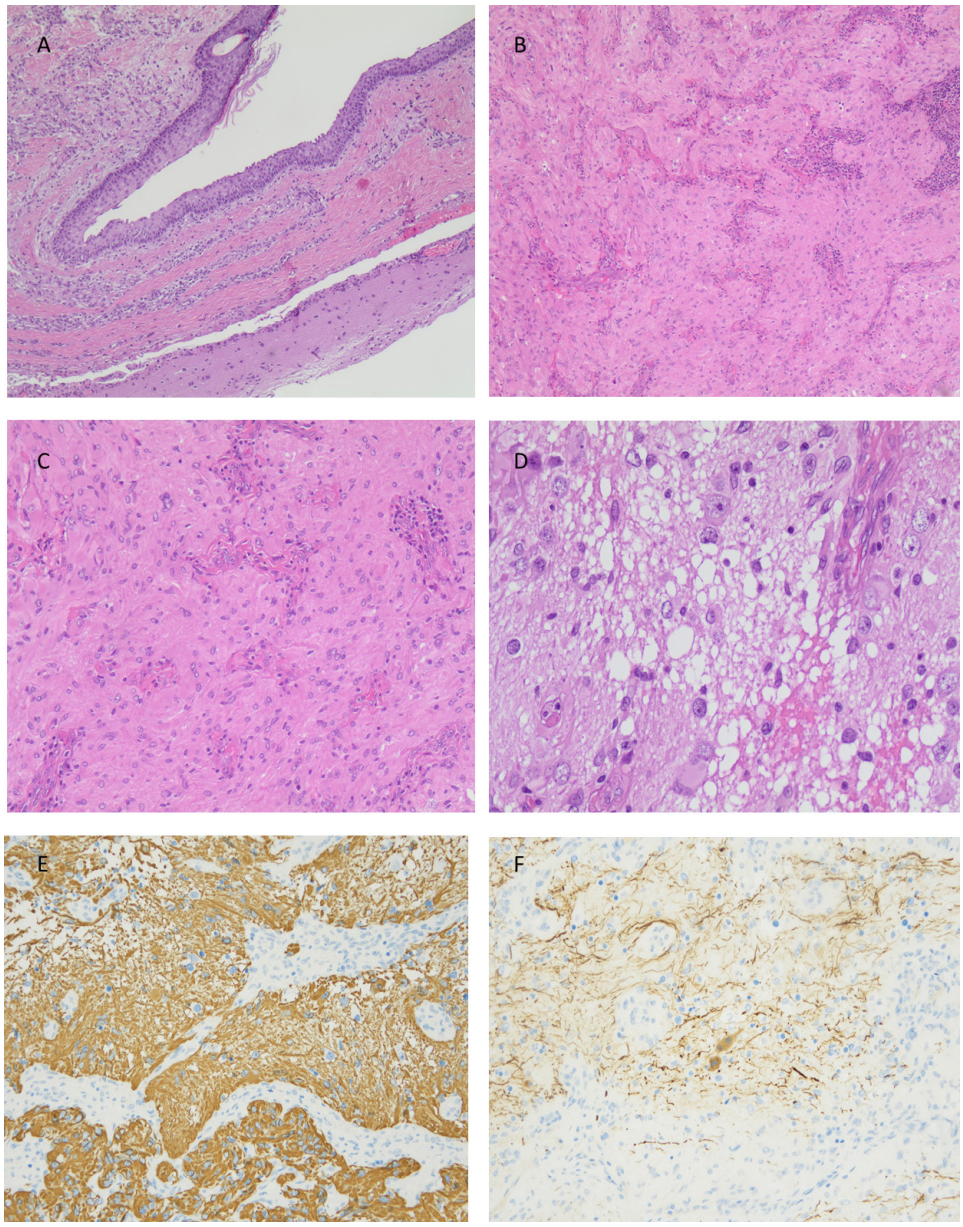

Figure 2 Histopathological features. The lesion showed the typical features of a mature teratoma formed by epithelial, neuroectodermal, and mesenchymal tissues. (A) A rim of nervous tissue bordered a squamous epithelial cyst within the teratomatous lesion. However, the teratoma showed areas formed by a proliferation of densely packed glial cells with intervening vascular stroma and lymphocytic infiltrates (B, C) where, in more loosely arranged areas, dysmorphic ganglion cells were also present (D). The glial cell component strongly expressed glial fibrillary acidic protein (GFAP) (E). The dysmorphic ganglion cells, sometimes also bi-nucleated, showed positive staining for neurofilament protein (F). (A–D: H&E staining; E: GFAP immunostaining; F: neurofilament protein immunostaining).

hereditary cancer syndromes (eg, Li Fraumeni, Cowden BRCA1/2), hormonal factors, and prior irradiation.[6] Further genotype/phenotype studies are needed to define a possible biological link between some unusual tumors (such as glioneuronal neoplasms, also in the setting of an ovarian teratoma) and BRCA1 mutation.[7]

There are no definite guidelines in the literature on the treatment of ovarian teratomas containing a neuroectodermal neoplasm. Treatment is generally surgical with chemotherapy and radiotherapy reserved for incomplete excisions or disseminated disease. It is difficult to evaluate the prognosis of patients with such tumors due to their extreme rarity. In our case, we adopted prudent patient management with careful clinical and radiological ultrasound-based follow-up.

CONCLUSION

In patients with a neuroectodermal-derived tumor within a mature teratoma a multidisciplinary management approach should be recommended due to the complexity of the pathological background and the rarity of such neoplasms.

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ORCID iDs
Angela Santoro http://orcid.org/0000-0002-6964-5152
Gian Franco Zannoni http://orcid.org/0000-0002-4473-7560

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