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Germ Cell Tumor with Somatic Transformation Successfully Treated with Combined Immunotherapy: A Case Report

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ABSTRACT

Germ cell tumors (GCTs) represent the most common malignancy in men between age 20 and 39 and are typically considered to be curable malignancies. Malignant somatic transformation (MST) is a well-recognized but rare phenomenon characterized by significant heterogeneity; consequently, its pathogenesis remains poorly understood. Available data, regarding prognosis and therapeutic management are also limited, while, based on current treatment strategies, radical surgical intervention continues to represent the mainstay of therapy.

Here, we present a case of a 49-year old male with a history of GCT, stage II, initially managed with left orchiectomy (1995), adjuvant cisplatin-based chemotherapy followed by selective excision of retroperitoneal lymph nodes, who developed a relapse 25 years later with evidence of MST and presence of an adenocarcinoma subtype.

Keywords: Malignant somatic transformation; Germ cell tumor; Adenocarcinoma; Retroperitoneal mass

INTRODUCTION

Germ cell tumors (GCTs) are potentially curable malignancies and demonstrate high response rates to chemotherapy, even in the metastatic disease setting. However, they exhibit a wide spectrum of differentiation, and in many cases they contain more than one histological subtype. The histological subtypes involved play a significant

role in therapeutic decision-making and demonstrate variable responses to chemotherapy and radiotherapy.[1-3]

The incidence of malignant somatic transformation (MST) has been reported in 2.7%–8.6% of non-seminomatous GCTs and may involve transformation into intestinal-type adenocarcinomas or, more commonly, sarcomatous transformation.[3-5] GCTs, with MST demonstrate intrinsic resistance to cisplatin- based chemotherapy regimens, and their management remains particularly challenging due to the absence of established treatment guidelines, reflecting the limited number of cases reported worldwide. Currently, the only known potentially curative treatment option is aggressive surgical management.[4,6]

CASE PRESENTATION

A 49-year-old male with a history of left non-seminomatous testicular cancer, diagnosed 30 years ago, was evaluated in our department. At the time of initial diagnosis in 1995, the patient underwent left orchiectomy, and histopathological examination revealed pure embryonal carcinoma of the testis. He subsequently received adjuvant chemotherapy consisting of 4 cycles of BEP (bleomycin, etoposide, cisplatin). Following completion of chemotherapy, selective excision of retroperitoneal lymph nodes was performed, revealing only fragments of necrotic tissue with no evidence of viable neoplastic cells. Postoperative staging work-up demonstrated no distant metastases. The clinical stage was II.

The patient was lost to follow-up with the medical oncology department for several years and subsequently presented for re-evaluation approximately four years ago. At that time, magnetic resonance imaging (MRI) of the abdomen demonstrated a para-aortic mass characterized by internal calcifications and associated adjacent lymphadenopathy, with a maximum measured dimension of 3.36 cm (Figure 1). The patient was not found to have any new co-morbidities and was asymptomatic, without fatigue, fever, nausea, abdominal pain, weight loss, or presence of any testicular mass. Laboratory evaluation revealed normal serum tumor markers, including alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β-hCG).

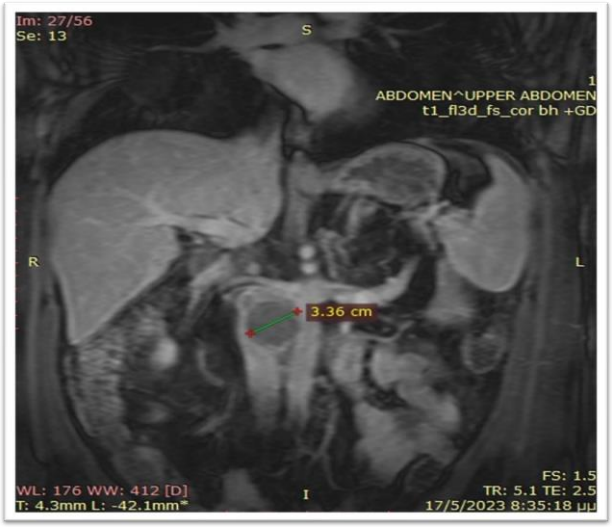

Figure 1: MRI corresponding image at diagnosis. Maximum measured dimension 3.36cm.

The para-aortic mass had remained stable over time; however, progressive enlargement of the adjacent lymph nodes was noted, prompting an image- guided lymph node biopsy. Histopathological analysis revealed a moderately differentiated adenocarcinoma, with morphologic (glands, often cribriform, with intraluminal dirty necrosis, lined by elongated stratified nuclei), and immunohistochemical (CK20, mCEA, CDX2 and SATB2 expression) features of intestinal differentiation (Figure 2). Subsequent positron emission tomography– computed tomography (PET/CT) demonstrated hypermetabolic retroperitoneal lymphadenopathy, with intense acidity and maximum standardized uptake value (SUVmax) of 7.2 (Figure 3).

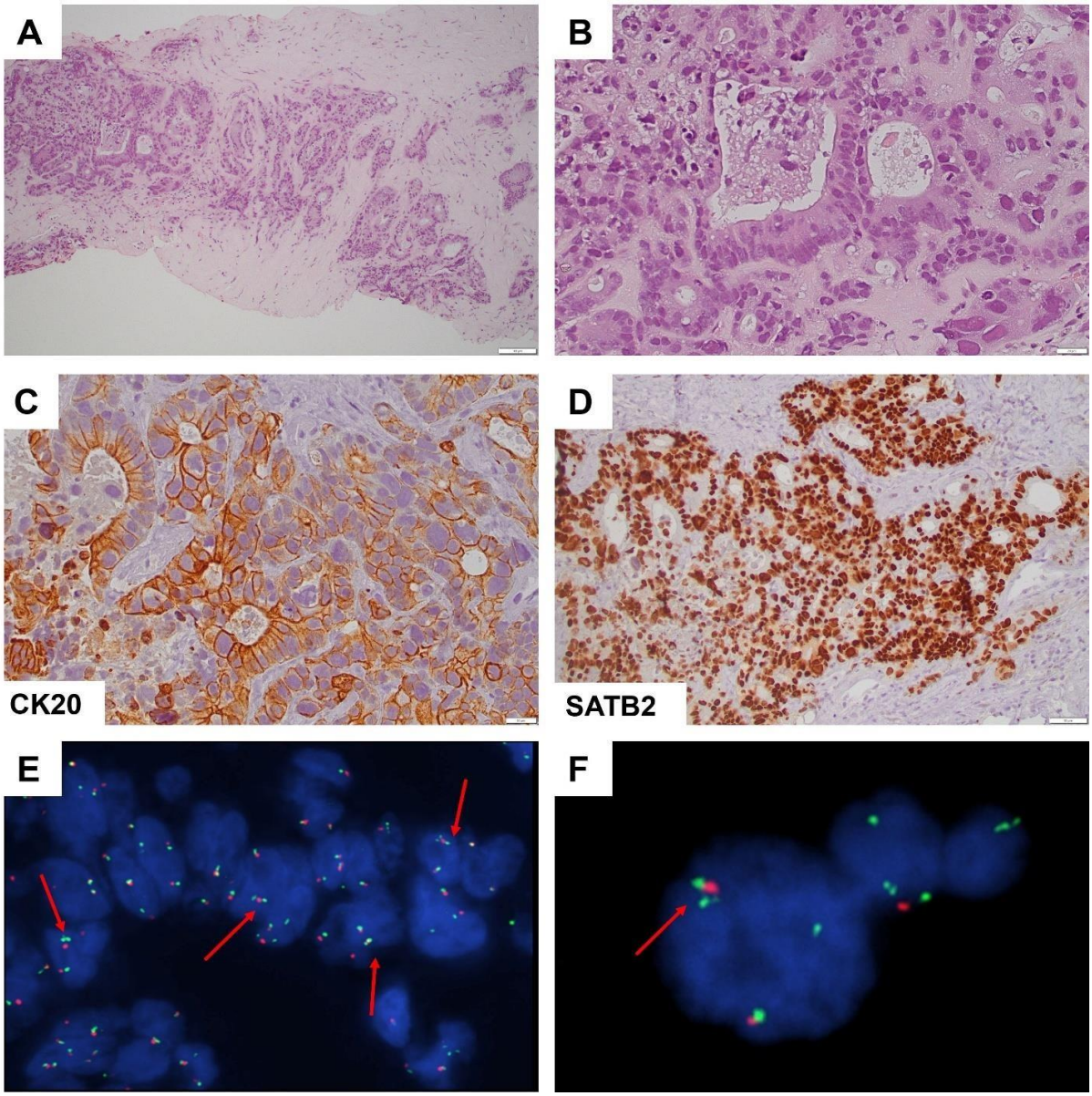

Figure 2: A. Microscopic examination shows a moderately differentiated adenocarcinoma composed of irregular glands with a cribriform and fused pattern. B. Higher magnification shows elongated pseudostratified pleomorphic nuclei, and intraluminal debris. High mitotic activity is present. C–D. Tumor cells express CK20 (C) and SATB2 (D), both markers of colonic differentiation. E-F. Interphase nuclei containing an i(12p) show a

green–red–green triplet pattern (arrows)

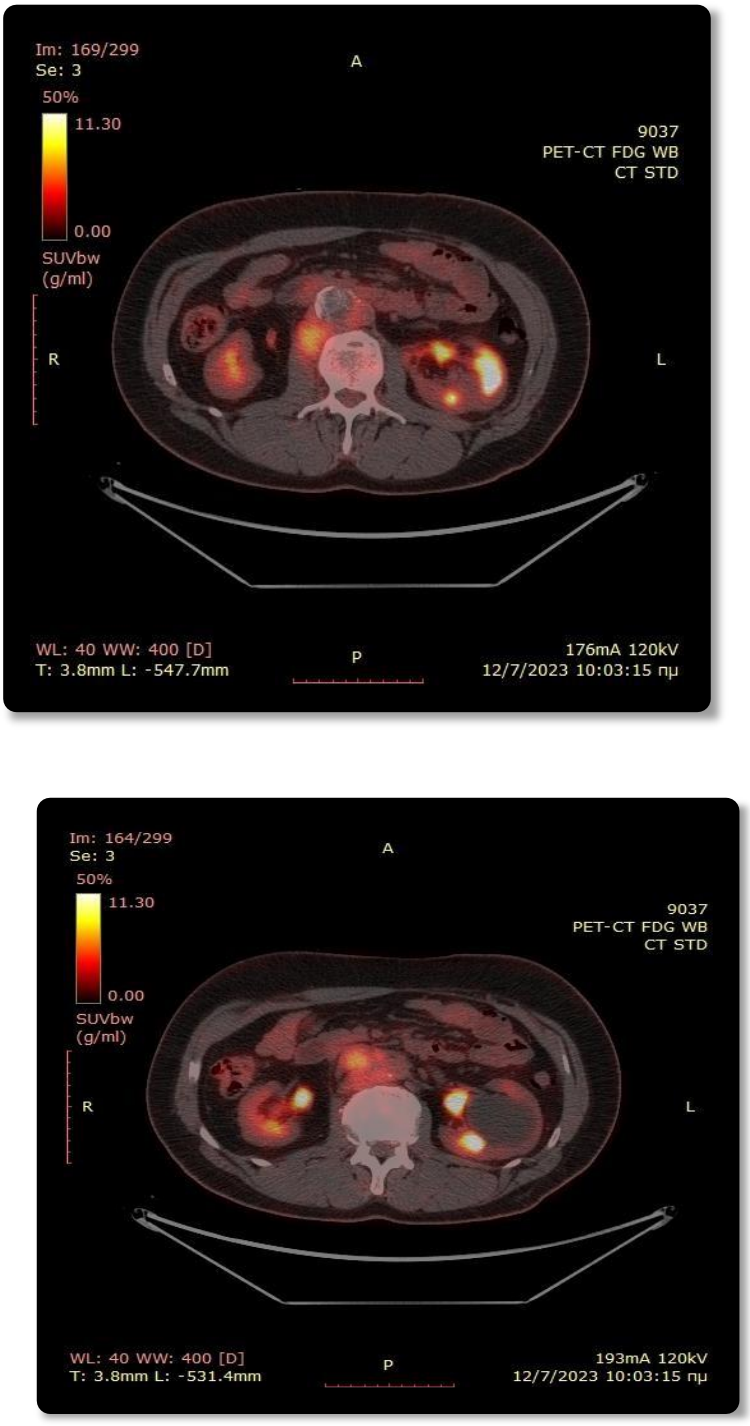

Figure 3: 18F-FDG PET/CT corresponding images at diagnosis. SUV max 7.2.

The patient underwent exploratory laparotomy with partial resection of the retroperitoneal lesion. Histopathology confirmed moderately differentiated intestinal-type adenocarcinoma, with immunomorphological features showing CK20 positivity and CK7 negativity. SALL 4 expression was not seen. The other markers were similar to the biopsy. Residual teratoma or other type of germ cell malignancy was not seen. In

light of the tumor's morphologic characteristics and immunohistochemical profile, and taking into account the patient's remote history of a germ cell tumor (>20 years prior) without evidence of residual or recurrent germ cell neoplasia, the possibility of a metastatic adenocarcinoma of colorectal origin was raised. However, colonoscopy and upper gastrointestinal endoscopy were subsequently performed and revealed no evidence of a primary gastrointestinal tumor.

Following the diagnosis of metastatic intestinal-type adenocarcinoma arising in the retroperitoneal lymph nodes, the patient received systemic chemotherapy with Capox (oxaliplatin and capecitabine) in combination with bevacizumab from February 2024 to June 2024, achieving a partial radiological response. Given the patient's prior history of testicular neoplasm, the diagnostic work-up was directed towards evaluating a possible relapse of the original germ cell tumor. Next-generation sequencing (NGS) was performed, revealing no actionable mutations, with only CTNNB1 and TP53 alterations detected. The tumor mutational burden was low at 4.21 mutations/Mb. Microsatellite instability was not revealed (MSS).
Formalin-fixed paraffin-embedded (FFPE) tissue blocks from the retroperitoneal lymph node biopsy were subsequently retrieved and send at the Molecular Diagnostics Unit, Department of Pathology, Ospedale San Raffaele, Milan. Molecular cytogenetic analysis using fluorescence in situ hybridization (FISH) demonstrated a hybridization pattern consistent with isochromosome i(12)(p10) in 95% of analyzed cells, confirming the diagnosis of metastatic relapse of a GCT with MST into an adenocarcinoma subtype.

Following completion of eight cycles of Capox, and after obtaining regulatory approval, the patient was initiated on maintenance immunotherapy with pembrolizumab in combination with bevacizumab in July 2024. This approach was pursued in the context of limited therapeutic options and despite the absence of microsatellite instability or increased mutational burden. Over the subsequent 19 months, the patient has continued maintenance therapy with bevacizumab and pembrolizumab, demonstrating overall partial disease response with no evidence of progression to date.

DISCUSSION

Testicular cancers are generally rare; however, they represent the most common malignancy among young men aged 20–39 years.[7] The majority are GCTs, which are further classified into seminomatous and non-seminomatous subtypes. Among non-seminomatous tumors, approximately 30%–50% contain more than one germ cell component and are therefore classified as mixed GCTs.[1] Overall, testicular cancers are considered potentially curable, with 5-year survival rates ranging from 80% to 95%, even in patients presenting with metastatic disease at diagnosis.[8,2] Nevertheless, relapse may occur in 10%–30% of patients despite initial complete treatment, and a small proportion may experience late relapse, defined as recurrence occurring at least two years after achieving an initial complete response.[9] A small subset of patients with GCTs may either harbor somatic-type malignancies at diagnosis or undergo transformation into somatic- type malignancies, namely malignant non–germ cell histologies that resemble carcinomas arising from other organs.[10]

As noted above, MSTs arising from GCTs are rare, with a reported incidence of 2.7%–8.6%, and are most

frequently observed in metastatic sites during late relapse.[3,11,12] Furthermore, MST appears to occur more commonly in patients who did not undergo initial retroperitoneal lymph node dissection (RPLND).[13] In the present case, the patient was subjected to partial removal of retroperitoneal lymph nodes, and this was performed as a secondary procedure following completion of chemotherapy.

Several studies have shown that these tumors exhibit chemoresistance; therefore, alternative therapeutic approaches, such as immunotherapy or targeted therapies, should be explored. Given the rarity of these cases, no established clinical guidelines exist, and therapeutic management is largely based on the resectability of the disease. Prognosis is variable and depends on multiple factors, including the timing of relapse, the site of relapse, and the histological subtype. Overall, prognosis appears to be poorer in cases with carcinomatous histology, metastatic disease, and late relapse.[7]

MST may arise either within the primary testicular tumor or at metastatic sites, even decades after the initial diagnosis. MST encompasses a broad spectrum of histological subtypes, most commonly sarcomas, followed by carcinomas and primitive neuroectodermal tumors (PNETs).[6,7,14] In rare instances, MST may manifest as carcinoid tumors, lymphomas, or nephroblastomas.[6,15] In a study of 63 cases, Hwang et al. reported that rhabdomyosarcoma was the most frequent histological subtype of MST arising in the primary testicular tumor, whereas adenocarcinoma predominated in cases in which MST occurred in metastatic disease.[16] In another study of 24 cases Scheckel et al. identified equal distribution between adenocarcinoma and sarcoma.[3]

As previously mentioned, MSTs may be observed even decades after the initial diagnosis of GCT; therefore, establishing an association with the primary tumor is often challenging. Establishing a germ cell origin is particularly difficult in metastatic GCTs that have undergone malignant somatic transformation. A thorough clinical history, together with adjunct immunohistochemical analyses, can aid in establishing the diagnosis. One potentially useful marker is SALL4; however, negative or weak expression does not exclude a germ cell origin. In our case, SALL4 expression was negative.

Isochromosome 12p [i(12p)] is detected in a high proportion of germ cell tumors (up to 89%) and represents a hallmark cytogenetic abnormality. Traditionally, its identification has relied on fluorescence in situ hybridization (FISH), a method that, while reliable, is technically demanding and time-consuming. More recently, quantitative real-time polymerase chain reaction (qRT-PCR) has been reported as a potential alternative approach for the detection of i(12p), offering advantages in terms of speed and feasibility in routine clinical practice.[17]

The optimal therapeutic strategy for GCTs with MST remains unclear. Several studies have reported relative resistance of MSTs to conventional GCT-directed chemotherapy, suggesting that therapy tailored to the somatic (transformed) component may be warranted. It remains debated whether systemic therapy should primarily target the transformed histology,[3,6,18] with some authors advocating GCT-oriented chemotherapy in combination with radical surgical resection, reserving histology-driven therapies for cases of recurrence.[7,14] In a case report by Pantaleo et al., complete radiological response was achieved with GCT-oriented chemotherapy

following prior therapy directed at the sarcomatous component, illustrating the potential efficacy of a flexible, individualized approach.[19] The role of radiotherapy in this setting also remains uncertain, whereas surgical resection, when feasible, continues to represent the cornerstone of management, regardless of disease stage.[7,19,20]

The timing of somatic transformation in germ cell tumors remains uncertain. Efforts have been made to identify potential prognostic factors for the development of GCTs with MST; however, the available evidence is largely derived from case reports and a limited number of small case series from specialized referral centers. In terms of prognosis, the 5-year overall survival (OS) for conventional GCTs reaches approximately 96% in non-metastatic disease and 80% in metastatic disease; however, survival for patients with MST declines substantially to approximately 50%–60%, reflecting the aggressive nature of this entity. Most studies to date have not demonstrated statistically significant differences in OS among the various histological subtypes of MST.[5,15]

Further molecular characterization, including the identification of potentially druggable biomarkers, may prove valuable in expanding therapeutic options for this highly heterogeneous group of neoplasms. To our knowledge, in the present case, immunotherapy was employed for the first time as maintenance treatment, with favorable clinical and radiological outcomes observed to date, highlighting a potential novel approach in the management of germ cell tumors with malignant somatic transformation.

CONCLUSION

GCTs with MST constitute a rare but clinically aggressive entity. Management of these tumors requires a multidisciplinary approach, including molecular characterization of the tumor for accurate diagnosis and biomarker identification, with surgical resection, systemic chemotherapy, and, when appropriate, targeted or immunotherapeutic strategies. Given the heterogeneous histology and molecular profiles of MST, further research is warranted to identify histology-specific targeted therapies and optimize patient outcomes.

REFERENCES

1. Cheville JC. Classification and pathology of testicular germ cell and sex cord- stromal tumors. Urol Clin North Am. 1999;26(3):595-609.
2. F K Mostofi. Proceedings: Testicular tumors. Epidemiologic, etiologic, and pathologic features. Cancer. 1973;32(5):1186-201.
3. Scheckel CJ, Kosiorek HE, Butterfield R, Ho TH, Hilal T. Germ Cell Tumors with Malignant Somatic Transformation: A Mayo Clinic Experience. Oncol Res Treat. 2019;42(3):95-100.
4. Little JS, Foster RS, Ulbright TM, Donohue JP. Unusual neoplasms detected in testis cancer patients undergoing post-chemotherapy retroperitoneal lymphadenectomy. J Urol. 1994;152(4):1144-1151.
5. Malagón HD, Valdez AMC, Moran CA, Suster S. Germ cell tumors with sarcomatous components: a clinicopathologic and immunohistochemical study of 46 cases. Am J Surg Pathol. 2007;31(9):1356-62.
6. R J Motzer, A Amsterdam, V Prieto, J Sheinfeld, V V Murty, M Mazumdar, et al. Teratoma with malignant transformation: diverse malignant histologies arising in men with germ cell tumors. J Urol. 1998;159(1):133-138.

7. Kevin R Rice, Martin J Magers, Stephen D W Beck, K Clint Cary, Lawrence H Einhorn, Thomas M Ulbright, et al. Management of germ cell tumors with somatic type malignancy: Pathological features, prognostic factors and survival outcomes. J Urol. 2014;192(5):1403-1409.
8. Brett S Carver, Angel M Serio, Dean Bajorin, Robert J Motzer, Jason Stasi, George J Bosl, et al. Improved clinical outcome in recent years for men with metastatic nonseminomatous germ cell tumors. J Clin Oncol. 2007;25(35):5603-5608.
9. Baniel J, Foster RS, Gonin R, Messemer JE, Donohue JP, Einhorn LH. Late relapse of testicular cancer. J Clin Oncol. 1995;13(5):1170-1176.
10. Mikuz G, Colecchia M. Teratoma with somatic-type malignant components of the testis. A review and an update. Virchows Arch. 2012;461(1):27-32.
11. C V Comiter, A S Kibel, J P Richie, M R Nucci, A A Renshaw. Prognostic features of teratomas with malignant transformation: a clinicopathological study of 21 cases. J Urol. 1998;159(3):859-63.
12. Washino S, Konishi T, Saito K, Ohshima M, Nakamura Y, Miyagawa T. Two cases of somatic-type malignancy as a very late relapse of testicular cancer successfully managed by surgical resection. J Surg case reports. 2017;2017(11).
13. Shilajit D Kundu, Darren R Feldman, Brett S Carver, Amit Gupta, George J Bosl, Robert J Motzer, et al. Rates of teratoma and viable cancer at post-chemotherapy retroperitoneal lymph node dissection after induction chemotherapy for good risk nonseminomatous germ cell tumors. J Urol. 2015;193(2):513-518.
14. Andrea Necchi, Maurizio Colecchia, Nicola Nicolai, Luigi Piva, Mario Catanzaro, Davide Biasoni,, et al. Towards the definition of the best management and prognostic factors of teratoma with malignant transformation: A single-institution case series and new proposal. BJU Int. 2011;107(7):1088-1094.
15. Charles C Guo, Metin Punar, Alejandro Luiña Contreras, Shi-Ming Tu, Louis Pisters, Pheroze Tamboli,, et al. Testicular germ cell tumors with sarcomatous components: an analysis of 33 cases. Am J Surg Pathol. 2009;33(8):1173-1178.
16. Hwang MJ, Hamza A, Zhang M, et al. Somatic-type Malignancies in Testicular Germ Cell Tumors: A Clinicopathologic Study of 63 Cases. Am J Surg Pathol. 2022;46(1):11-17.
17. Fichtner A, Richter A, Filmar S, et al. The detection of isochromosome i(12p) in malignant germ cell tumours and tumours with somatic malignant transformation by the use of quantitative real-time polymerase chain reaction. Histopathology. 2021;78(4):593-606.
18. Alessia C Donadio, Robert J Motzer, Dean F Bajorin, Philip W Kantoff, Joel Sheinfeld, Jane Houldsworth,, et al. Chemotherapy for teratoma with malignant transformation. J Clin Oncol. 2003;21(23):4285-4291.
19. Pantaleo MA, Mandruzzato M, Indio V, et al. Case Report: The Complete Remission of a Mixed Germ Cell Tumor With Somatic Type Malignancy of Sarcoma Type With a GCT-Oriented Therapy: Clinical Findings and Genomic Profiling. Front Oncol. 2021;11(March):1-9.
20. Mustafa OM, Mohammed SF, Aljubran A, Saleh WN. Immature mediastinal teratoma with unusual histopathology: A case report of multi-lineage, somatic-type malignant transformation and a review of the literature. Medicine (Baltimore). 2016;95(26):e3378.