REDAK SLUČAJ INICIJALNO POGREŠNO DIJAGNOSTIKOVANOG MEŠOVITOG MALIGNOG GERMINATIVNOG TUMORA MEDIJASTINUMA, ODSTRANJENOG „COLISEUM" PRISTUPOM

PRIKAZ SLUČAJA

CASE REPORT

A RARE CASE OF PRIMARILY MISDIAGNOSED GIANT MALIGNANT MIXED GERMINATIVE MEDIASTINAL TUMOR IN A YOUNG MALE PATIENT, SURGICALLY REMOVED BY "COLISEUM" APPROACH

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SAŽETAK

Uvod: Mešoviti tumor germinativnih ćelija (MGCT) najčešće se javlja kod mlađih pacijenata i primarno je lokalizovan u gonadama. Nakon pregleda dostupne literature zaključili smo da postoji samo nekoliko opisanih slučajeva medijastinalnog MGCT-a. Primarni medijastinalni MGCT čini približno 10–15% svih maligniteta medijastinuma i do 3% svih mešovitih tumora germinativnih ćelija. U dostupnoj literaturi do sada nije opisan medijastinalni MGCT sa više od tri patološke komponente, kao što su tumor žumančane kese, teratom i embrionalni karcinom. Kod našeg pacijenta bile su prisutne još dve dodatne komponente – horiokarcinom i seminom.

Prikaz slučaja: Pacijent muškog pola, starosti 40 godina, javio zbog bola u grudima i povišene telesne temperature. CT grudnog koša pokazala je ogromnu tumorsku masu u desnom hemitoraksu dijametra 120 mm. Bronhoskopski nalaz bio je uredan, a transbronhijalne biopsije negativne. Primenjen je kombinovani otvoreni i VATS pristup, nakon čega je postavljena dijagnoza nemikrocelularnog karcinoma pluća (NSCLC). Pacijent je lečen hemioterapijom, ali je kontrolni CT grudnog koša pokazao progresiju bolesti. Doneta je odluka o hirurškom lečenju – planirana je salvage pneumonektomija primenom „coliseum" pristupa. Intraoperativno je potvrđeno da tumor potiče iz medijastinuma, te je u potpunosti odstranjen. Celo desno plućno krilo bilo je u atelektazi, ali bez infiltracije tumorskim tkivom, pa je tokom operacije postignuta potpuna reekspanzija desnog pluća. Pacijent je dobro podneo operativni zahvat. Definitivni patohistološki nalaz pokazao je da se radi o mešovitom malignom tumoru germinativnih ćelija. Urološki pregled i postoperativni CT pregled celog tela nisu pokazali znake rezidualnog ili recidivantnog tumora.

Zaključak: Pacijent je inicijalno pogrešno dijagnostikovan i lečen hemioterapijom nakon procene da nije kandidat za hirurško lečenje. Prvobitno planirana salvage operacija kod ovog mladog pacijenta završila se radikalnim operativnim zahvatom bez potrebe za izvođenjem pneumonektomije.

Ključne reči: mešoviti tumor germinativnih ćelija medijastinuma, pogrešno dijagnostikovan NSCLC, „coliseum" pristup, tumori medijastinuma, hirurško lečenje

ABSTRACT

Introduction: Mixed germ cell tumor (MGCT) is most common in younger patients and is localized primarily to the gonads. After reviewing the literature, we concluded that there are only a few cases of mediastinal MGCT – primary mediastinal MGCT accounts for about 10-15% of all mediastinal malignancies and up to 3% of all MGCT. Mediastinal MGCT with more than three pathological components, such as yolk sac tumor, teratoma, and embryonal carcinoma, has not been reported previously in the reviewed literature. Our patient had two more components (carcinoma and seminoma).

Case report: The patient was a 40-year-old male who presented with chest pain and fever; chest CT showed a giant mass in the right pleural space, with a maximal diameter of 120 mm. Bronchoscopic findings were normal, and bronchial biopsies were negative. A combined open and VATS approach was used, which revealed NSCLC. The patient underwent chemotherapy, but the next CT scan of the thorax showed progression. Decision was made to perform surgical treatment – salvage pneumonectomy with "coliseum" approach. Intraoperatively, it was verified that the tumor origins were in the mediastinum, so the whole tumor was removed. The whole right lung was in atelectasis, but was not infiltrated by tumor – full reexpansion of the right lung was established during the surgery. The patient tolerated surgery well. Definitive PH finding showed that it was a mixed malignant germinative tumor. Urology findings and the postoperative full-body CT showed no signs of residual or recurrent tumor.

Conclusion: The patient was initially misdiagnosed and treated with chemotherapy after the conclusion that he was not a candidate for surgical treatment. Primarily planned salvage surgery for this young patient ended as radical surgery and without the need for pneumonectomy.

Keywords: mixed germ cell tumor of mediastinum, misdiagnosed NSCLC, Coliseum approach, mediastinal tumors, surgical treatment

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UVOD

Mešoviti tumori germinativnih ćelija retko se javljaju van gonada. U literaturi je opisan ograničen broj slučajeva medijastinalnih mešovitih tumora germinativnih ćelija, manje od deset, a do sada nije prijavljen nijedan slučaj medijastinalnog mešovitog tumora germinativnih ćelija koji sadrži više od tri histopatološke komponente [1]. Mešoviti tumor germinativnih ćelija definiše se prisustvom najmanje dve različite komponente tumora germinativnih ćelija i uglavnom ga karakteriše nizak stepen ćelijske diferencijacije [2]. Ovi tumori pretežno nastaju u gonadama, najčešće u jajnicima mladih žena i testisima mladih muškaraca. Pojava na ekstragonadalnim lokalizacijama je retka, a među opisanim mestima javljanja nalaze se medijastinum, regija glave i vrata i trbušna duplja. Među ekstragonadalnim tumorima germinativnih ćelija, prednji medijastinum predstavlja najčešću lokalizaciju i obuhvata približno 50–70% slučajeva [3]. Kliničke manifestacije su različite i najčešće uključuju nelagodnost u grudima, kašalj, otežano disanje, povišenu telesnu temperaturu, noćno znojenje i gubitak telesne mase [4]. Izbor terapijske strategije zavisi od histološkog sastava tumora i najčešće podrazumeva samostalnu hiruršku resekciju ili hemioterapiju zasnovanu na cisplatini, nakon koje sledi operativno lečenje.

Kod našeg pacijenta dijagnostikovan je mešoviti medijastinalni tumor germinativnih ćelija sastavljen od pet komponenti: tumora žumančane kese, postpubertetskog teratoma, embrionalnog karcinoma, horiokarcinoma i seminoma.

PRIKAZ SLUČAJA

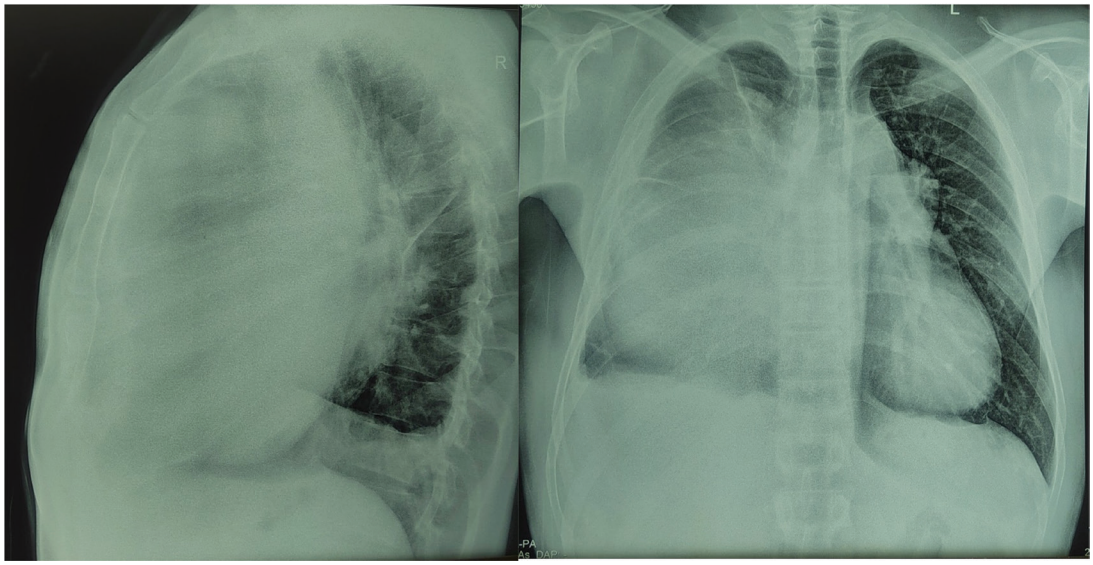
Naš pacijent bio je muškarac star 40 godina, nepušač, bez prethodne istorije hroničnih bolesti, kod koga se bolest manifestovala trnjenjem desne šake, povišе-

INTRODUCTION

Mixed germ cell tumors rarely occur outside the gonad. A limited number of cases, fewer than 10 of mediastinal mixed germ cell tumors have been documented in the literature, and no previous reports have described a mediastinal MGCT containing more than three histopathological components [1]. A mixed germ cell tumor is defined by the presence of at least two distinct germ cell tumor components and is generally characterized by poor cellular differentiation [2]. These tumors predominantly arise in the gonads, most commonly in the ovaries of young women and the testes of young men. Occurrence at extragonadal sites is uncommon, with reported locations including the mediastinum, head and neck region, and abdominal cavity. Among extragonadal germ cell tumors, the anterior mediastinum represents the most frequent site, accounting for approximately 50–70% of cases [3]. Clinical manifestations are variable and commonly include chest discomfort, cough, shortness of breath, fever, nocturnal sweating, and weight loss [4]. The tumor's histological composition guides treatment strategies and generally consists of surgical resection alone or cisplatin-based chemotherapy followed by surgery. Our patient had a mixed mediastinal germ cell tumor which had five components – Yolk Sac tumor, Teratoma postpubertale, Carcinoma embryonale, Choriocarcinoma, and Seminoma.

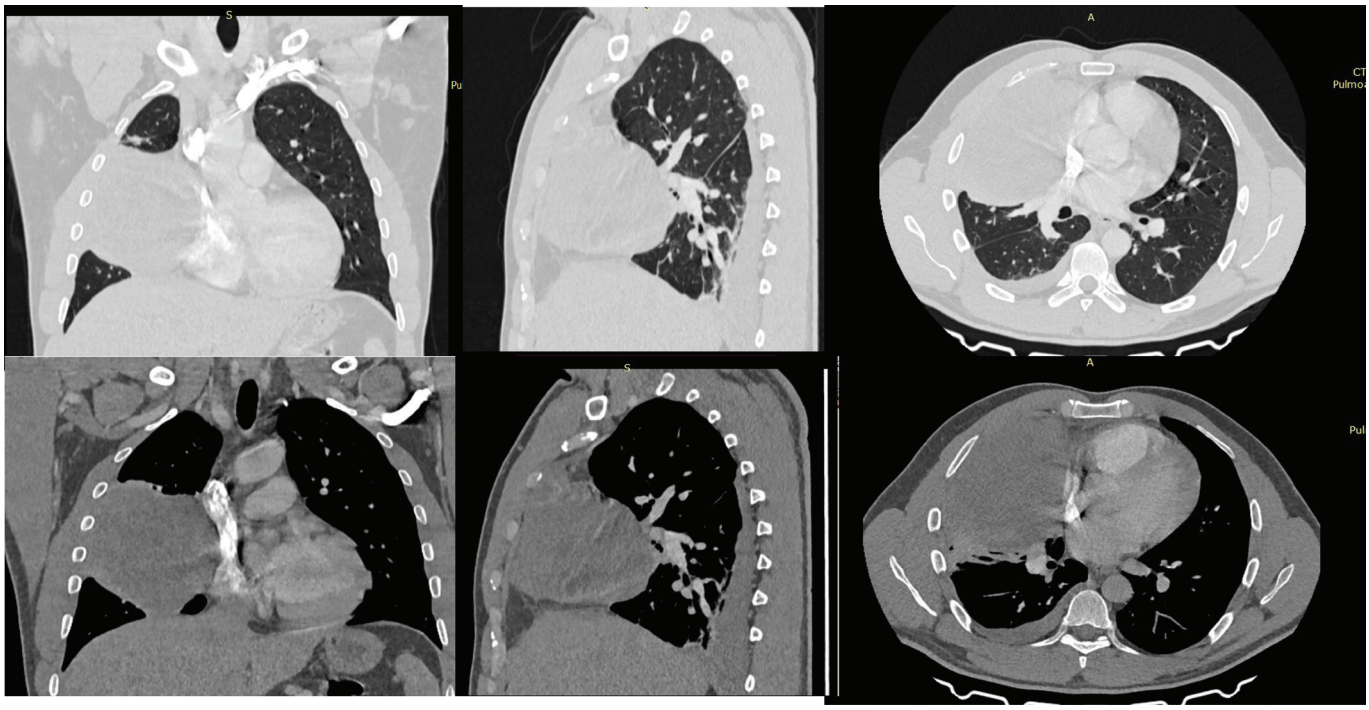
CASE REPORT

Our patient was a 40-year-old man, a non-smoker and with no previous history of chronic diseases, in whom the disease manifested in the form of tingling in the right hand, fever, and a feeling of shortness of breath. The patient was hospitalized in the home institution



Slika 1. Rentgen grudnog koša na prijemu

Figure 1. Chest X-ray on admission



Slika 2. CT grudnog koša – prikaz velike tumorske mase u desnom pleuralnom kavumu, sa kompresijom na strukture medijastinuma

Figure 2. Chest CT showing a large tumor in the right pleural space, with compression to mediastinal structures

nom telesnom temperaturom i osećajem nedostatka vazduha. Pacijent je hospitalizovan u matičnoj ustanovi zbog bola u grudima koji je trajao nekoliko dana pre prijema.

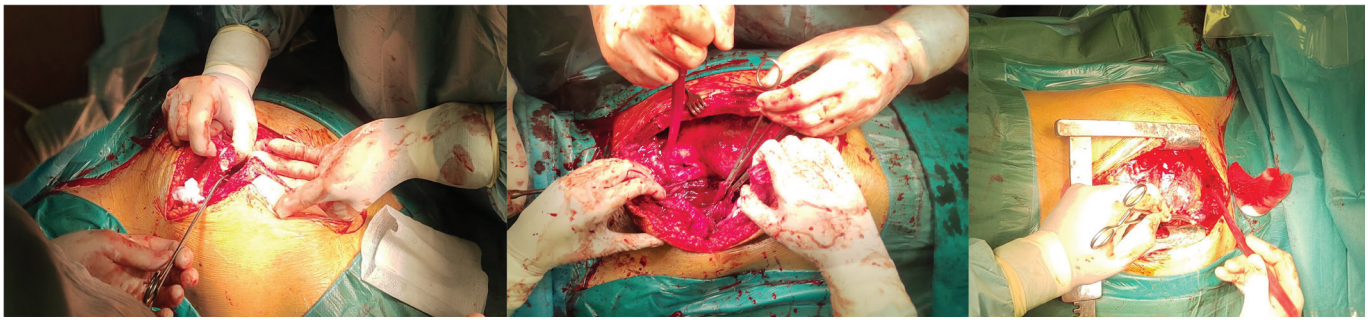
Po prijemu su urađeni radiografija grudnog koša (Slika 1) i multislajsna kompjuterizovana tomografija (MSCT) grudnog koša (Slika 2). U prednjem delu desnog hemitoraksa uočena je kolekcija tečnosti koja je dovela do atelektaze prednjih delova plućnog parenhima. Opisana kolekcija bila je dimenzija 95 × 85 × 120 mm i potiskivala je medijastinalne strukture ulevo.

Sedam dana nakon prijema doneta je odluka o izvođenju VATS eksploracije, ali to nije bilo moguće zbog izraženih priraslica za grudni zid. Urađena je konverzija u desnostranu minitorakotomiju sa parcijalnom adheziolizom i biopsijom, a uzorci su poslati na definitivni patohistološki pregled.

Definitivni patohistološki nalaz ukazao je na prisustvo nemikrocelularnog karcinoma pluća neuroendokrinog porekla (Large cell carcinoma neuroendocrines pulmonis). Pacijent je prikazan Onkološkom konzilijumu iste ustanove, nakon čega je doneta odluka o nastavku lečenja hemioterapijom prema EP protokolu.

Pacijent je primio dva od četiri planirana ciklusa hemioterapije. Kako nije bilo znakova poboljšanja, nakon drugog ciklusa urađen je kontrolni CT grudnog koša, koji je pokazao progresiju tumora do veličine od 153 mm, sa kompresijom srca i medijastinalnih struktura ulevo, kao i nastankom kompresivne atelektaze plućnog parenhima.

due to chest pain that had been going on for several days before admission. Upon admission, chest X-ray (Figure 1) and MSCT of the chest (Figure 2) were performed. In the anterior aspect of the right hemithorax, a collection of fluid was found, resulting in atelectasis of the anterior lung parenchyma. The described collection measured 95 mm x 85 mm x 120 mm and was pushing the mediastinal structures to the left. Seven days after admission, the decision was made to proceed with VATS exploration, but this was impossible due to strong adhesions to the chest wall. Conversion to right minithoracotomy was done with partial adhesiolysis and biopsy, and the samples were sent for a definitive PH examination. Definitive PH finding showed the presence of non-small cell lung cancer – neuroendocrine origin (Large cell carcinoma neuroendocrines pulmonis). The patient was presented to the Oncology Consilium at the same institution – a decision was made to proceed with further chemotherapy according to the EP regimen. The patient received two of the four indicated chemotherapy cycles. With no signs of improvement, control chest CT was indicated and done after the second cycle of chemotherapy – it showed progression in the size of the tumor to 153 mm, which led to compression of the heart and mediastinal structures to the left, and which creates compressive atelectasis of the lung parenchyma. The patient sought a second opinion at our institution one month later. We performed another chest CT scan, which was identical to the previous one. The patient was then admitted to



Slika 3. *„Coliseum"* pristup – sternotomija u kombinaciji sa desnom torakotomijom kroz četvrti međurebarni prostor. Velika medijastinalna masa vrši invaziju desne brahiocefalične vene

Figure 3. "Coliseum" approach – sternotomy combined with right thoracotomy through the fourth intercostal space. Huge mediastinal tumor invading the right brachiocephalic vein

Mesec dana kasnije pacijent se javio u našu ustanovu radi dobijanja drugog mišljenja. Ponovljen je CT pregled grudnog koša, čiji je nalaz bio identičan prethodnom. Nakon toga pacijent je primljen na našu Kliniku radi hirurškog lečenja. Pri prijemu bio je febrilan i žalio se na suv, nadražajan kašalj, kao i osećaj stezanja i bola u desnom hemitoraksu.

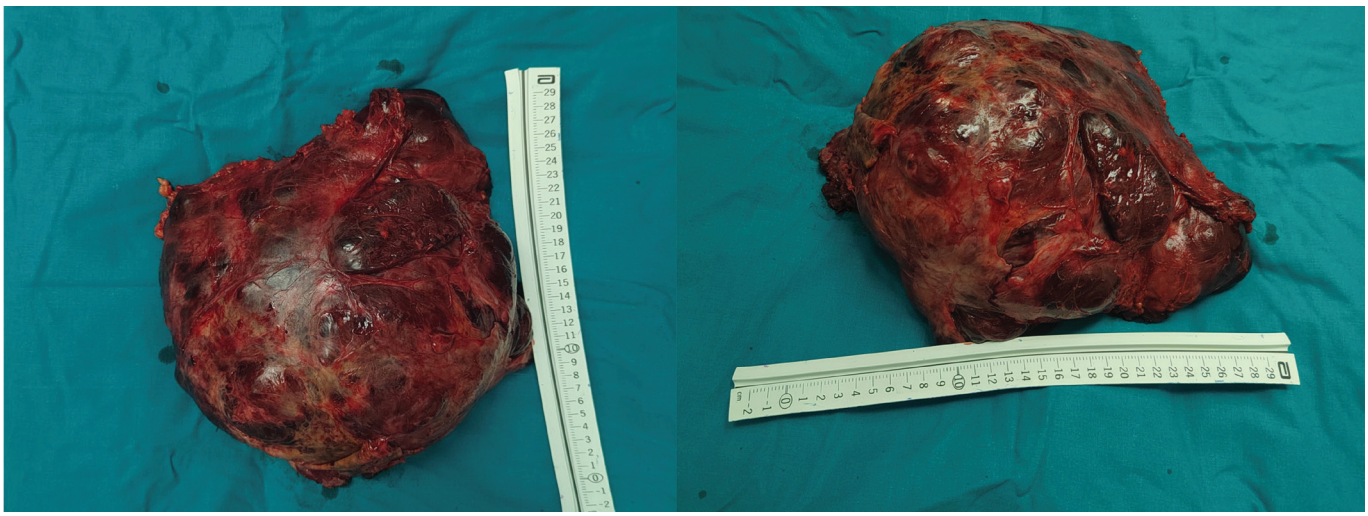
Po prijemu je sprovedena kompletna klinička i laboratorijska obrada. Smatrali smo da je hirurško lečenje najbolja opcija za ovog mladog pacijenta, međutim veličina tumora i potencijalna hemodinamska nestabilnost tokom lateralnog dekubitusa neophodnog za izvođenje torakotomije uslovili su izbor drugačijeg hirurškog pristupa. Doneta je odluka o izvođenju salvage pneumonektomije primenom „coliseum" pristupa [5] – kombinovane sternotomije i desnostrane torakotomije, koju je prvi opisao prof. Tristan Yan (Slika 3).

Pacijent je postavljen u ležeći položaj na leđima, nakon čega je urađena sternotomija uz istovremenu torakotomiju kroz četvrti međurebarni prostor. U medijastinumu i desnoj pleuralnoj šupljini uočena je velika tumorska masa. Intraoperativno je potvrđeno

our Clinic for surgical treatment. On admission, he was febrile and complained of a dry, irritating cough and a feeling of tightness/pain in the right hemithorax.

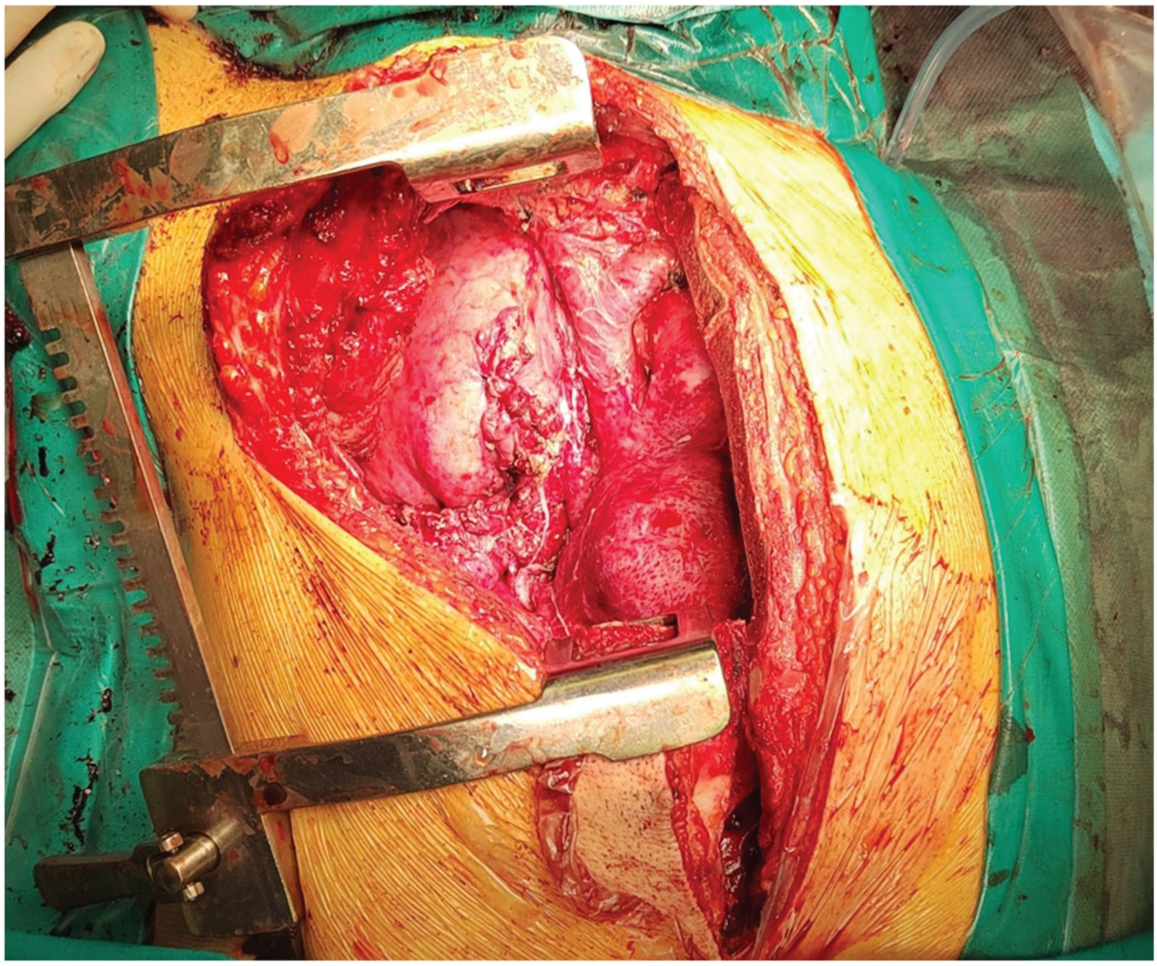
Upon admission, the patient underwent a complete clinical and laboratory examination; we assumed that the surgical treatment was the best option for his young patient, but the size of the tumor and potential hemodynamic instability during the lateral decubitus needed for thoracotomy dictated another surgical approach. We decided to perform salvage pneumonectomy with the "coliseum" approach [5] – combined sternotomy and right thoracotomy, firstly described by Prof. Tristan Yan (Figure 3).

The patient was positioned supine, and a sternotomy was performed with a combined thoracotomy through the fourth intercostal space. A large mediastinal mass was seen in the mediastinum and right pleural space. Intraoperatively, it was verified that the origin of the tumor was in the mediastinum, so the entire tumor was removed. During the preparation, the iatrogenic injury of the right brachiocephalic vein was treated with a PDS suture (Figure 3). After removal of the tumor (Figure 4), the entire right lung was in atelectasis, but



Slika 4. Uklonjeni tumor medijastinuma

Figure 4. Removed mediastinal tumor



Slika 5. Desni pleuralni prostor i desna strana medijastinuma nakon uklanjanja tumora, sa kompletnom reekspanzijom desnog pluća

Figure 5. Right pleural space and right side of mediastinum after removal of the tumor, with complete reexpansion of the right lung

da tumor potiče iz medijastinuma, te je u potpunosti odstranjen.

Tokom preparacije došlo je do jatrogene povrede desne brahiocefalične vene, koja je uspešno zbrinuta PDS šavom (Slika 3). Nakon uklanjanja tumora (Slika 4), celo desno plućno krilo bilo je u atelektazi, ali bez infiltracije tumorskim tkivom. Sa visceralne pleure uklonjena je fibrinska kora, čime je tokom operacije postignuta potpuna reekspanzija desnog pluća (Slika 5). Postavljen je jedan dren u desnu pleuralnu šupljinu i jedan dren u medijastinum.

Postoperativni tok protekao je uredno. Pacijent je ekstubiran neposredno nakon operacije, uz uredan nalaz gasnih analiza arterijske krvi. Radiografija grudnog koša pokazala je potpunu reekspanziju desnog plućnog krila. Medijastinalni dren uklonjen je drugog postoperativnog dana, a pleuralni trećeg postoperativnog dana, bez znakova pleuropulmonalnih komplikacija.

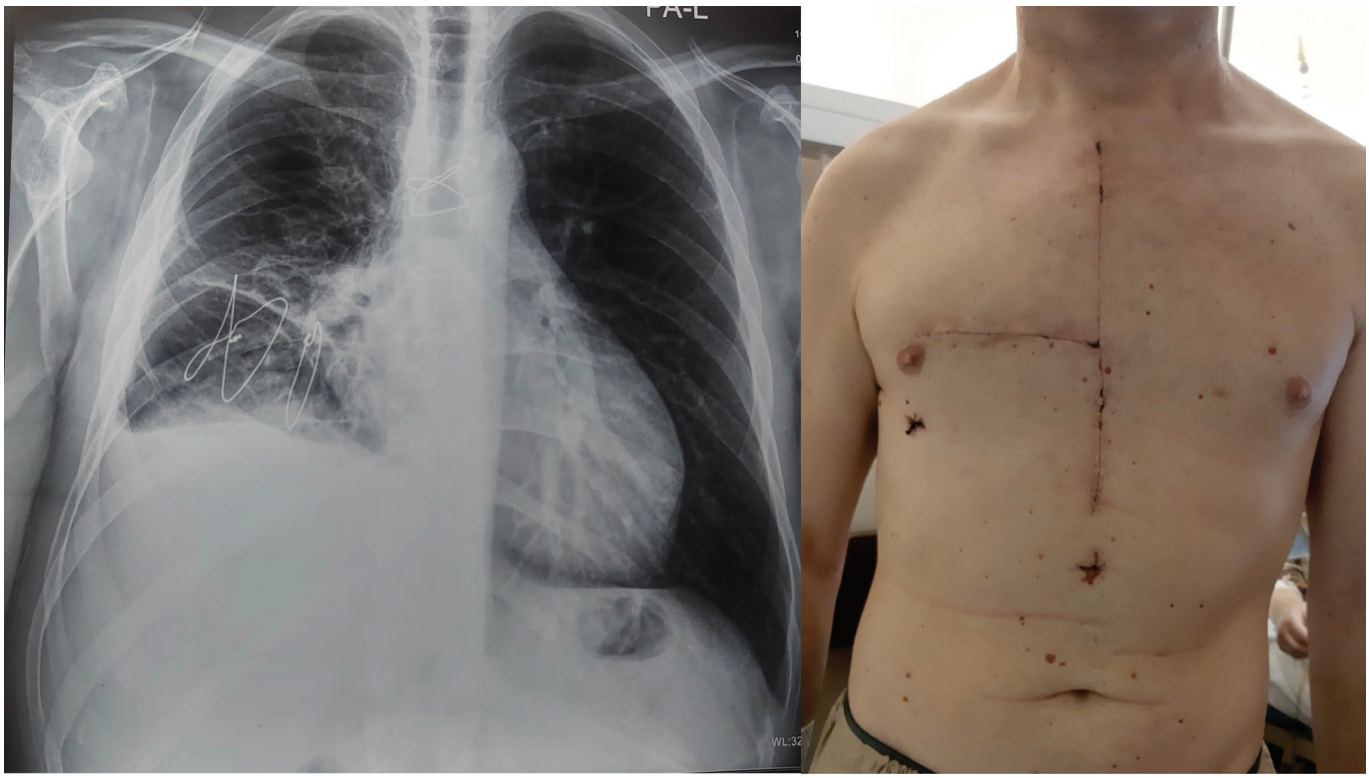
Pacijent je dobro podneo operativni zahvat i otpušten je na dalje kućno lečenje u dobrom opštem stanju, afebrilan i sa urednim lokalnim nalazom (Slika 6).

not infiltrated by the tumor. The fibrinous cortex was removed from the visceral pleura, and a complete reexpansion of the right lung was established during the operation (Figure 5). One drain was placed in the right pleural space, and one in the mediastinum.

The postoperative course went well. The patient was extubated immediately after surgery, with a good arterial blood gas analysis. Chest X-ray showed complete reexpansion of the right lung. The mediastinal tube was removed on the second postoperative day, and the pleural on the third postoperative day, with no signs of pleuropulmonary complications.

The patient tolerated the operation well and was discharged for further home treatment in good general condition, afebrile, with normal local findings (Figure 6).

The definitive PH finding showed a mixed malignant germinative cell tumor (Yolk sac tumor 40% + Teratoma postpubertale 30% + Carcinoma embryonale 10% + Choriocarcinoma 10% + Seminoma 10%). Urological examination and postoperative MSCT of the whole body revealed the absence of tumor rest/recurrence.



Slika 6. levo – Rentgen grudnog koša prilikom otpusta, desno – incizija kod „Coliseum" pristupa

Figure 6. Left – chest X-ray after removal of chest tubes – last day of hospitalization, right – Incision of the "coliseum" approach – 7 days after surgery

Definitivni patohistološki nalaz pokazao je mešoviti maligni tumor germinativnih ćelija (Yolk sac tumor 40% + Teratoma postpubertale 30% + Carcinoma embryonale 10% + Choriocarcinoma 10% + Seminoma 10%). Urološki pregled i postoperativni MSCT celog tela nisu pokazali prisustvo rezidualnog tumora niti znakove recidiva bolesti.

DISKUSIJA

Mešoviti maligni tumori germinativnih ćelija medijastinuma relativno su retki i čine 1–3% svih malignitеta germinativnih ćelija i približno 15% medijastinalnih maligniteta germinativnih ćelija. Češće se javljaju kod muškaraca (oko 97%) i uglavnom pogađaju mlađe pacijente [6]. Etiologija ekstragonadalnog porekla ovih tumora i dalje nije u potpunosti razjašnjena.

Teratom predstavlja najzastupljeniji histološki podtip medijastinalnih tumora germinativnih ćelija i javlja se kod približno 44% obolelih. Većina medijastinalnih tumora germinativnih ćelija pripada neseminomskoj grupi i čini oko 70% svih slučajeva, dok seminomi čine približno 30% dijagnoza [7,8]. Histološki podtip u velikoj meri određuje terapijski pristup, koji može obuhvatati neposrednu hiruršku resekciju ili multimodalno lečenje koje uključuje hemioterapiju praćenu hirurškim odstranjenjem tumora.

DISCUSSION

Mixed malignant germinative cell tumors of the mediastinum are relatively rare, with an incidence of 1–3% of all germ-cell malignancies and approximately 15% of mediastinal ones. They are more common in men (about 97%) and occur more often in younger patients [6]. The etiology of non-gonadal origin remains unclear.

Teratoma is the most prevalent histological subtype of mediastinal germ cell tumor, occurring in nearly 44% of affected individuals. The majority of mediastinal germ cell tumors are non-seminomatous, comprising approximately 70% of cases, while seminomas account for about 30% of diagnoses [7,8]. The histological subtype largely guides therapeutic management and may involve either direct surgical resection or multimodal treatment consisting of chemotherapy followed by surgical excision.

Mediastinal germ cell tumors of the non-seminomatous subtype are associated with an unfavorable prognosis and are therefore classified as high risk [9]. By comparison, teratomas and seminomatous tumors are considered good- or intermediate-risk entities, depending on marker concentrations and the extent of disease dissemination at the time of diagnosis.

Neseminomski medijastinalni tumori germinativnih ćelija povezani su sa nepovoljnom prognozom i zbog toga se svrstavaju u grupu tumora visokog rizika [9]. Nasuprot tome, teratomi i seminomski tumori smatraju se tumorima dobrog ili srednjeg rizika, u zavisnosti od koncentracije tumorskih markera i stepena proširenosti bolesti u trenutku postavljanja dijagnoze.

Terapijsko lečenje seminomskih medijastinalnih tumora germinativnih ćelija zasniva se na proceni rizika i najčešće uključuje tri ili četiri ciklusa hemioterapije bleomicinom, etopozidom i cisplatinom (BEP). Nasuprot tome, neseminomski tumori se obično leče indukcionom hemioterapijom nakon koje sledi hirurška resekcija. Četiri ciklusa (BEP) protokola predstavljaju najčešće primenjivani terapijski režim. Dodatni hirurški zahvati mogu biti korisni kod odgovarajuće odabranih pacijenata zbog pozitivnog uticaja na dugoročno preživljavanje. Radioterapija ostaje alternativna terapijska opcija kod bolesnika sa rezidualnim lezijama lokalizovanim u neposrednoj blizini vitalnih organa [4].

Kod našeg pacijenta dijagnostikovan je mešoviti maligni medijastinalni tumor germinativnih ćelija sastavljen od pet različitih komponenti: tumor žumančane kese 40%, postpubertetski teratom 30%, embrionalni karcinom 10%, horiokarcinom 10% i seminom 10%. Shodno tome, dominantan deo tumora činile su neseminomske komponente, koje su povezane sa nepovoljnim prognostičkim faktorima i slabijim odgovorom na hemioterapiju. Hemioterapija je sprovedena prema režimu sličnom prethodno opisanom, ali bez kliničkog i radiološkog odgovora. Nakon detaljne analize CT snimaka celog tela i isključivanja ekstratorakalnog širenja bolesti, kao i imajući u vidu iznenađujuće dobar nalaz spirometrije, doneta je odluka o izvođenju salvage operacije – desnostrane pneumonektomije primenom „coliseum" pristupa, koji je procenjen kao najbolja opcija za pacijenta, bez ugrožavanja hemodinamske stabilnosti koja bi mogla nastati tokom lateralnog dekubitusa.

Pacijent je inicijalno pogrešno dijagnostikovan kao bolesnik sa nemikrocelularnim karcinomom pluća i lečen hemioterapijom nakon procene da nije kandidat za hirurško lečenje. Prvobitno planirana salvage operacija kod ovog mladog pacijenta završila se radikalnim operativnim zahvatom bez potrebe za izvođenjem pneumonektomije.

Sukob interesa: Nije prijavljen.

Therapeutic management of seminomatous mediastinal germ cell tumors is determined by risk stratification and typically includes three or four cycles of bleomycin, etoposide, and cisplatin (BEP) chemotherapy. In contrast, non-seminomatous tumors are usually treated with induction chemotherapy followed by surgical resection. Four cycles of (BEP) represent the most frequently used regimen. Additional surgical procedures may be beneficial for suitable candidates due to their positive impact on long-term survival. Radiotherapy remains an alternative option for patients with residual lesions located in proximity to vital organs [4].

Our patient had a mixed malignant germinative cell mediastinal tumor, which consisted of five different components: Yolk sac tumor 40% + Teratoma postpubertale 30% + Carcinoma embryonale 10% + Choriocarcinoma 10% + Seminoma 10%; thus, this tumor mostly consisted of non-seminomatous components, which are associated with poor prognostic factors and poor response to chemotherapy as well. Chemotherapy was administered according to a regimen similar to the previously noted one, with no clinical or radiological response. With a complete review of CT scans (full body CT) and exclusion of extrathoracic propagation of disease and surprisingly good spirometry findings, we decided to perform a salvage surgery – right pneumonectomy, with "coliseum" approach as the best option for the patient, without having to compromise hemodynamics as in lateral decubitus.

The patient was initially misdiagnosed as non-small cell lung carcinoma and treated with chemotherapy after the conclusion that he was not a candidate for surgical treatment. Primarily planned salvage surgery for this young patient ended as radical surgery and without the need for pneumonectomy.

Conflict of interest: None declared.

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