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CASE REPORT
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Ewing sarcoma with initial presentation in mandible – a case report

Srđan Milanović[1], Nikola Milošević[1], Marko Dožić[1], Dušan Ristić[1], Goran Stojković[2], Nebojša Miletić[1]

[1]Institute for Oncology and Radiology of Serbia, Belgrade, Serbia;
[2]Clinical Center of Serbia, Clinic for Otorhinolaryngology and Maxillofacial Surgery, Belgrade, Serbia

SUMMARY

Ewing sarcoma is a tumor that rarely occurs after the age of twenty. This tumor is even more rare in the region of head and neck, either as a primary site or a place of dissemination of the disease. Treatment is multidisciplinary and includes administration of chemotherapy, surgery and/or radiotherapy. This case report refers to the 29-year-old female patient who was referred to maxillofacial surgeon for tooth pain and swelling of the left side of mandible that was not solved after the antibiotic treatment. After a biopsy was performed, Ewing's sarcoma of the mandible was diagnosed, and primary localization in the pelvis was confirmed before starting the treatment. One year after chemotherapy and radiation treatment completion, there was no sign of disease. This case shows that all doctors specialized in oral and / or maxillofacial surgery, as well as medical doctors and dentists in primary health care, have important role in early diagnosis of these rare diseases, and thus contribute to better treatment outcomes, even in advanced cases.

Keywords: Ewing sarcoma; mandible; chemotherapy; radiotherapy

INTRODUCTION

Ewing sarcoma is a rare disease. Incidence of sarcomas in adults are less than 1% of all solid tumors, and only about 10% of them are localized in bones [1]. Ewing sarcoma (ES) in population of children and young adults is on the second place of bone tumor by frequency. Ewing sarcoma group of tumors includes Ewing sarcoma in bone, extraosseus Ewing sarcoma and Askin tumor (PNET). ES is usually diagnosed in the second decade, while in the first decade appears in about 20–30% of these tumors. Occurrence after 30 years of age is rare [2].

Ewing sarcoma may occur in any bone, however, most often appears in long and flat bones, in the first place with localization in pelvis, femur, chest bones, tibia, fibula and humerus. Its manifestation in the head bones is not common, either as a primary site, or as a site of dissemination of the disease, with a prevalence of 2% [3], and the most commonly affected is mandible [4].

These tumors are primarily manifested as pain and swelling, but as lesions grow there is disfunction of the affected region. At the time of diagnosis, about 25% of patients have metastasis, but only about 10% of patients present with isolated bone metastases [3]. Patients with localized disease have better prognosis with survival rate of about 60 - 70%, while patients with metastasis at initial diagnosis have significantly worse prognosis with a survival rate of less than 25% [3].

The treatment is multimodal and includes chemotherapy, surgery and radiotherapy, with an active cooperation of members of a multidisciplinary oncological team [3, 5].

CASE REPORT

A female patient 29 years old visited a dentist in January 2017, due to pain and swelling of the left side of mandible, in good general health, with no other symptoms. She was administered wide-spectrum antibiotic, but no improvement has been achieved. The patient was then refered to maxillofacial surgeon at the Clinical Center of Serbia.

Initial CT exam of the head and neck showed osteolysis of the left ramus, irregularly shaped (Figure 1). Biopsy was performed at the beginning of February 2017. After receiving histopathological findings, patient was presented on the specialist tumor board for sarcoma and admitted to the Institute for Oncology and Radiology of Serbia for additional diagnosis and starting chemotherapy.

Additional examinations (CT neck, chest, abdomen and pelvis, MR pelvis, SCI skeleton, X-ray) revealed the presence of osteolytic tumor mass in the right iliac bone with extension to the right sacroiliac joint and infiltration of the sacrum cortex, as well as minor exstraskeletal propagation and infiltration of gluteus maximus muscle, with total dimensions of 2×9 cm. There were also other osteolytic lesions found in the sacrum (4×2, 7×2 cm) with lateral reaching to the left sacroiliac joint and one more lesion in the left iliac bone, above acetabulum (1.5×1.5 cm).

The treatment started with VIDE (vincristine, ifosfamide, doxorubicin, etoposide) regimen chemoterapy. After six cycles of chemotherapy, the control CT examinations showed regression of the disease (Figure 2) and the control PET CT (September 2017) showed the absence of increased metabolism of the radiopharmaceutical (complete

Address for correspondence: Srđan MILANOVIĆ, Institute for Oncology and Radiology of Serbia, 14 Pasterova St., Belgrade, Serbia; *srdjan_milanovitch@yahoo.com*

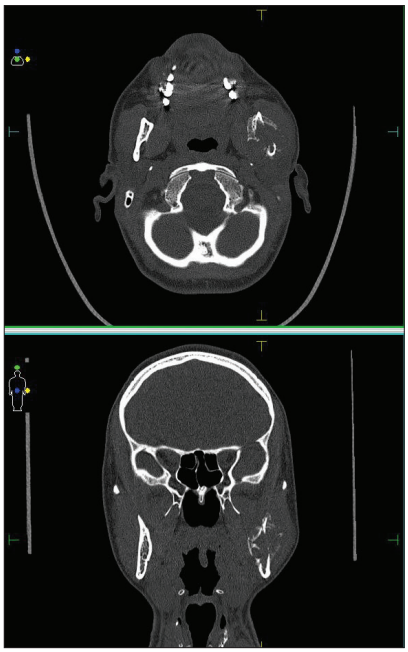

Figure 1. Tumor of mandibular ramus – Initial CT of the head and neck
Slika 1. Tumor ramusa mandibule – Inicijalni CT glave i vrata

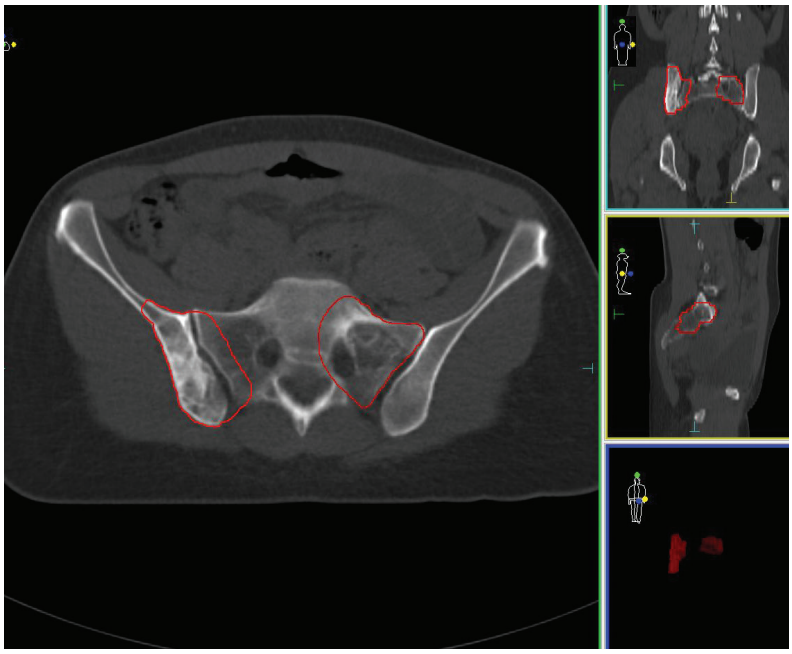

Figure 2. The primary localization of tumor in pelvis, CT after CT VIDE
Slika 2. Primarna lokalizacija tumora u karlici, CT nakon HT VIDE

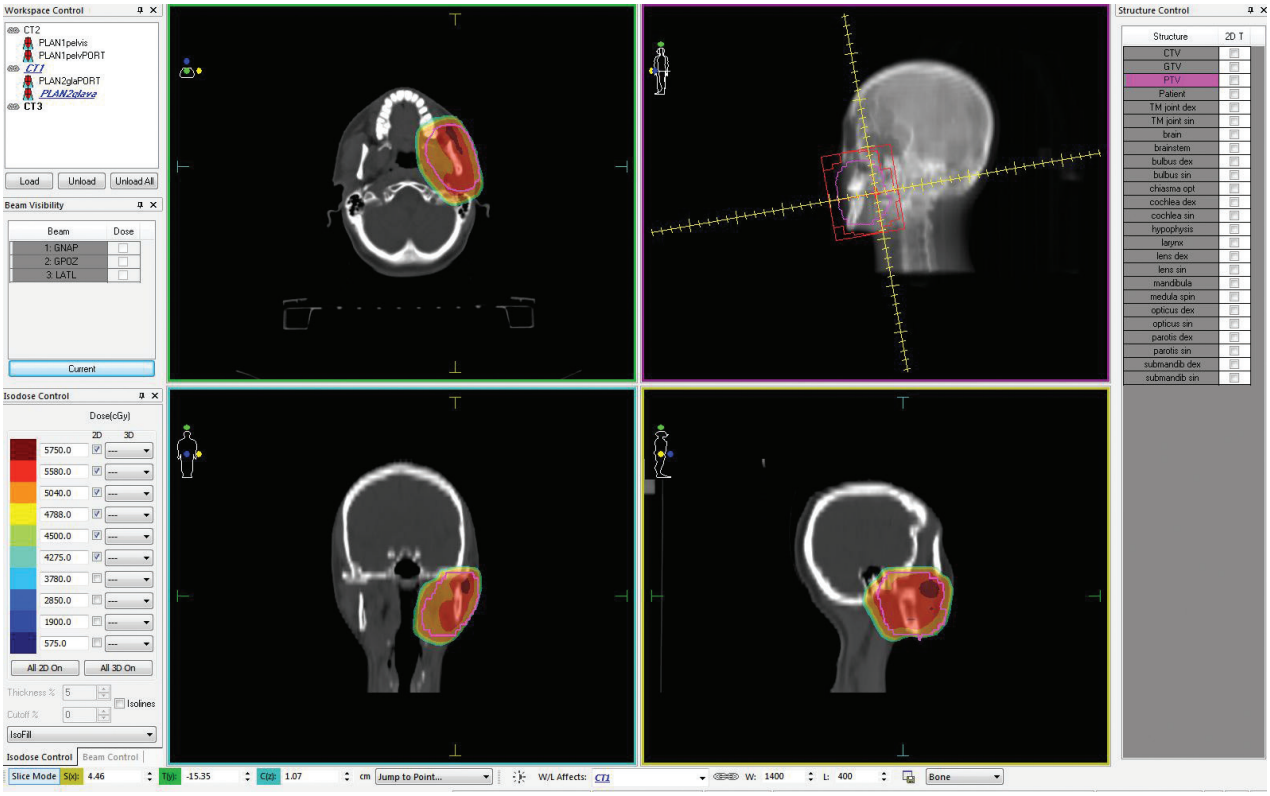

Figure 3. The treated volume and dose distribution in mandible localization
Slika 3. Tretirani volumen i dozna distribucija lokalizacije u mandibuli

response, CR). The patient was then presented to the tumor board and radiotherapy of initially affected locations as well as continuing of chemotherapy with VAI (vincristine, actinomycin, ifosfamide) was prescribed.

Radiation therapy was planned as 3D conformal technique (3DCRT) with standard regime of fractionation 1.8 Gy / day with total dose TD 55.8 Gy in 31 fractions in the region of mandible (Figure 3) and TD 50.4 Gy in 28 fractions of the pelvic region. Radiotherapy was conducted in February 2018 with good subjective tolerance, but with development of radiomucositis grade 1 and radiomucositis grade 2 in the left buccal area, that eventually healed

after increased local care. The administration of chemotherapy VAI (eight cycles) was completed in May 2018. Control PET CT scan in July 2018 confirmed complete response, and the tumor board indicated regular checkups.

At the last control checkup in May 2019, there were no signs of recurrence, the patient had no simptoms, and no toxicity was demonstrated one year after completion of combined treatment and more than two years from diagnosis.

DISCUSSION

Ewing's sarcoma is a rare tumor that is most common in the population under the age of 15 years, while rarely occurs in population over 30 years old and younger than 5 years. The appearance of the disease in the region of head and neck is especially rare and it includes about 2% of all cases of Ewing's sarcoma [2, 3].

In our case report, the first manifestation of the disease was tooth pain and swelling of the left side of mandible. Such initial presentation of the disease was likely the reason for postponing early diagnoses, which may have negative influence on the course of the disease and treatment [4].

Taking into account that in our case patient was in good general health, with no signs and symptoms that would indicate the existence of tumors in pelvis, timely refering to maxillofacial surgery has contributed to rapid initiation of diagnosis and treatment.

Despite the fact that Ewing's sarcoma in maxillofacial, and head and neck region is rare, this case indicates that all medical doctors and dentists in primary health care and doctors who specialise in oral and / or maxillofacial surgery, have very important role in early diagnosis of these rare diseases, and thus can contribute to better treatment outcomes, even in advanced cases.

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Juingov (Ewing) sarkom sa inicijalnom prezentacijom u mandibuli – prikaz slučaja

Srđan Milanović[1], Nikola Milošević[1], Marko Dožić[1], Dušan Ristić[1], Goran Stojković[2], Nebojša Miletić[1]

[1]Institut za onkologiju i radiologiju Srbije, Beograd, Srbija;
[2]Klinički centar Srbije, Klinika za otorinolaringologiju i maksilofacijalnu hirurgiju, Beograd, Srbija

KRATAK SADRŽAJ

Juingov (Ewing) sarkom je tumor koji se retko javlja posle dvadesete godine života. Pojavljivanje ovog tumora u regiji glave i vrata je još ređe, bilo kao primarno mesto ili kao mesto diseminacije bolesti. Lečenje je multidisciplinarno i uključuje primenu hemoterapije, hirurgiju i/ili radioterapiju. Prikaz slučaja se odnosi na pacijentkinju staru 29 godina koja je upućena maksilofacijalnom hirurgu zbog bola zuba i otoka leve strane donje vilice, koji nije prolazio posle primene antibiotika. Nakon biopsije je dijagnostikovan Juingov sarkom u mandibuli, a pre otpočinjanja lečenja je potvrđena primarna lokalizacija u karlici. Posle godinu dana od kompletirane hemoterapije i radioterapije nema znakova bolesti. Ovaj slučaj ukazuje da svi lekari koji su specijalizovani za oralnu i/ili maksilofacijalnu hirurgiju, kao i doktori medicine i stomatologije, u primarnoj zdravstvenoj zaštiti mogu imati izuzetno važnu ulogu u što ranijoj dijagnozi ove retke bolesti, a samim tim doprineti boljim rezultatima lečenja, čak i kod uznapredovalih slučajeva.

Ključne reči: Juingov (Ewing) sarkom; mandibula; hemoterapija; radioterapija

UVOD

Juingov sarkom (JS) retko je oboljenje.

Kod odraslih sarkomi broje manje od 1% slučajeva svih solidnih tumora, a od toga je samo oko 10% tumora lokalizovano u kostima [1]. JS je u populaciji dece i mladih odraslih na drugom mestu po učestalosti koštanih tumora. U grupi JS, osim koštanog JS, postoje još ekstraosealni JS i Askinov tumor. JS se najčešće dijagnostikuje u drugoj deceniji, dok se u prvoj deceniji javlja oko 20–30 % slučajeva ovih tumora. Pojavljivanje posle 30. godine je retko [2].

JS se može javiti u bilo kojoj kosti; međutim, najčešće se javlja u dugim i pljosnatim kostima, na prvom mestu sa lokalizacijom u kostima karlice, femuru, kostima grudnog koša, potkolenice i humerusu. Pojavljivanje u kostima glave nije uobičajeno, bilo kao primarno mesto ili kao mesto diseminacije bolesti, sa učestalošću oko 2% [3], i tada je najčešće zahvaćena mandibula [4].

Ovi tumori se najpre manifestuju pojavom bola i otoka, a sa rastom promene dolazi i do poremećaja funkcije zahvaćene regije. U trenutku dijagnoze je oko 25% pacijenata sa prisutnim metastazama, a samo kod oko 10% pacijenata se javljaju izolovane metastaze u kostima [3]. Pacijenti sa lokalizovanom bolešću imaju bolju prognozu, sa stopom preživljenja oko 60–70 %, dok pacijenti sa inicijalno prisutnim metastazama imaju znatno lošiju prognozu, sa stopom preživljenja manjom od 25% [3].

Lečenje je multimodalno, zasnovano na hemoterapiji (HT), hirurgiji i radioterapiji, u aktivnoj saradnji članova multidisciplinarnog onkološkog tima [3, 5].

PRIKAZ SLUČAJA

Pacijentkinja stara 29 godina javila se svom stomatologu u januaru 2017. godine zbog bola i otoka leve strane donje vilice. Bila je dobrog opšteg zdravlja, bez drugih tegoba. Tada je ordiniran antibiotik širokog spektra, na čiju primenu nije došlo do promene kliničke slike. Pacijentkinja je zatim upućena maksilofacijalnom hirurgu u Klinički centar Srbije.

Inicijalni CT glave i vrata je pokazao osteolizu levog ramusa mandibule, nepravilnih kontura (Slika 1), te je početkom februara 2017. učinjena biopsija tumora. Po dobijenom histopatološkom nalazu pacijentkinja je prikazana konzilijumu za sarkome i primljena u Institut za onkologiju i radiologiju Srbije radi dodatne dijagnostike i otpočinjanja lečenja primenom hemoterapije. Na učinjenim pregledima (CT vrata, grudnog koša, abdomena i karlice, MR karlice, SCI skeleta, RTG) pokazano je prisustvo osteolitične tumorske mase tela desne ilijačne kosti sa zahvatanjem desnog sakroilijačnog zgloba i infiltracijom korteksa krila sakruma, kao i manjom ekstraosealnom propagacijom i infiltracijom *m. gluteus maximusa*, dimenzija 2 × 9 cm. Takođe je u sakrumu bila prisutna druga osteolitična lezija 4 × 2,7 × 2 cm, koja lateralno dopire do levog sakroilijačnog zgloba, i još jedna promena 15 × 15 mm supraacetabularno u levoj ilijačnoj kosti.

Lečenje je otpočeto primenom HT po protokolu VIDE (vinkristin, ifosfamid, doksorubicin, etopozid). Nakon šest ciklusa HT, kontrolni CT pregledi su pokazali regresiju bolesti (Slika 2), a kontrolni PET CT (septembar 2017) ukazao je na odsustvo pojačanog metabolizma radiofarmaka, odnosno kompletan odgovor (CR), te je pacijentkinja prikazana konzilijumu kada je indikovana radioterapija inicijalno zahvaćenih lokalizacija, kao i primena HT po šemi VAI (vinkristin, aktinomicin, ifosfamid).

Zračna terapija je planirana 3D konformalnom tehnikom, standardnim režimom frakcionisanja 1,8 Gy/dnevno sa TD 55,8 Gy u 31 frakciji na predeo mandibule (Slika 3) i TD 50,4 Gy u 28 frakcija na predeo pelvisa. Radioterapija je sprovedena februara 2018. godine uz dobru subjektivnu toleranciju, uz razvoj radiomukozitisa gr 1 i radiomukozitisa gr 2 levo bukalno, koji su sanirani uz pojačanu lokalnu negu.

Primena HT po šemi VAI (osam ciklusa) kompletirana je maja 2018. godine, a kontrolni PET CT od jula 2018. je potvrdio kompletan odgovor, te je konzilijum indikovao redovne kontrole.

Na poslednjoj kontroli u ranom toku praćenja, koja je bila maja 2019. godine, nema znakova recidiva, pacijentkinja je bez novih tegoba i bez ispoljene toksičnosti godinu dana nakon sprovedenog kombinovanog lečenja i više od dve godine od postavljanja dijagnoze.

DISKUSIJA

JS je redak tumor koji se najčešće javlja u populaciji starosti do 15 godina, dok se kod starijih od 30 godina i mlađih od pet godina retko dijagnostikuje. Pojavljivanje ove bolesti u regiji glave i vrata je posebno retko jer se JS u kostima glave nalazi samo u oko 2% od svih slučajeva JS [2, 3].

U našem prikazu slučaja je prva manifestacija bolesti bila bol zuba i otok leve strane donje vilice. Takva inicijalna prezentacija bolesti lako može dovesti do odlaganja pravovremene dijagnoze, što može imati loš uticaj na lečenje i tok bolesti ovih agresivnih tumora [4].

Imajući u vidu da je u našem slučaju pacijentkinja bila dobrog opšteg zdravlja, klinički bez simptoma i znakova koji bi upućivali na postojanje tumora u karlici, pravovremeno upućivanje maksilofacijalnom hirurgu doprinelo je brzom postavljanju dijagnoze i otpočinjanju lečenja.

Uprkos tome što se JS u maksilofacijalnoj i regiji glave i vrata retko javlja, ovaj slučaj ukazuje da svi doktori medicine i stomatologije u primarnoj zdravstvenoj zaštiti, kao i lekari koji su specijalizovani za oralnu i/ili maksilofacijalnu hirurgiju, imaju izuzetno važnu ulogu u što ranijoj dijagnozi ove retke bolesti, a samim tim mogu doprineti boljim rezultatima lečenja, čak i kod uznapredovalih slučajeva.