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### Case Series of Rare Head and Neck Plasmacytoma: Experiences in Indonesia

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#### ABSTRACT

**Background:** Solitary plasmacytoma (SP) is a rare case of plasma cell neoplasms, which only represent 5-10% of all plasma cell neoplasms that afflict two or three people per every 100,000 of the general population. This neoplasm is divided into solitary plasmacytoma of the bone (SBP) and solitary extramedullary plasmacytoma (SEP), depending on the location. Due to the rarity, SBP can be misdiagnosed as multiple myeloma (MM) while SEP as plasma cell granuloma, whereas the treatments are very different. This study aimed to present our experiences in diagnosing SP in the head and neck to differentiate them from MM and plasma cell granuloma. **Case presentation:** One case of multiple solitary plasmacytomas of the bone (SPB) in the frontal bone and one case of intraoral solitary extramedullary plasmacytoma (SEP) were presented. The SBP showed abnormality in the laboratory and the CT showed a punch-out lesion which is similar to MM. The SEP showed normal laboratory findings, but the histopathology mimicked plasma cell granuloma. Both immunohistochemistry was positive for CD138, and the SEP diagnosis was confirmed by Ki67 and  $\kappa$ -light chain. Complete examination from history taking, physical examination, radiology and laboratory findings, bone marrow morphology, and histopathology including immunohistochemistry examination, are very important to determine the correct diagnosis. **Conclusion:** the case was diagnosed as head and neck solitary plasmacytoma.

#### 1. Introduction

Plasma cell disorders are monoclonal neoplasms that originate from B lymphocyte lineage. It consists of several groups, and the most common disease is multiple myeloma (MM).<sup>1</sup> MM is a cytogenetically heterogeneous clonal plasma cell proliferative disorder and is almost always preceded by an asymptomatic premalignant stage. There are several premalignant stages of MM, and one of the rarest is solitary plasmacytoma (SP).<sup>2</sup> Solitary plasmacytoma (SP) is a rare variant of myeloma characterized by a localized

accumulation of monoclonal plasma cells without any evidence of systemic plasma cell proliferative disorder and only accounts 5-10% of all plasma cell neoplasms and 2-5% of all plasma cells disorders.<sup>3-5</sup> In the United States, the total incidence of SBP was 0.45/100,000 persons, and SEP was 0.12/100,000 persons during the 2013-2016 period.<sup>6</sup> Incidence in the Asian population is lower than the African American and Caucasian with a median age at diagnosis of both SBP and SEP is 55 years old with age range 26-87 years and male to female ratio is 2:1 to 4:1.<sup>3,7,8</sup> <sup>3-5</sup> The

incidence of solitary plasmacytoma in Indonesia is unknown, but several case reports had been reported.<sup>8,9</sup> Regarding the location and originate tissue, plasmacytoma is divided into 2 groups, solitary plasmacytoma of the bone (SBP) and solitary extramedullary plasmacytoma (SEP) which each disease has different clinical presentations and characteristics. SBP originates from bones and mostly occurs in the bones of axial skeleton such as vertebra and skull. SBP presents as a lytic bone lesion without bone marrow plasmacytosis and approximately 60% of SBP could progressed to MM within 3 years. SEP is less common than SBP and 80% occurs in upper respiratory tracts such as nasal cavity, sinuses, nasopharynx and larynx. SEP usually presents in the predilection area without marrow plasmacytosis and rarely recur or progress to MM. According to International Myeloma Working Group Diagnostic Centre for Multiple Myeloma and Related disorders, 10% to 30% of SEP could progress to MM within 3 years.<sup>1-5,10</sup>

Both plasmacytomas are highly responsive to local radiation therapy.<sup>1,3-5</sup> The confirmed diagnosis is mandatory to exclude MM because the prognosis and treatment of MM and SP vary greatly.<sup>11</sup> Patients with MM require chemotherapy and symptomatic therapy to prevent complication of the diseases, while patients with SP require radiation therapy as treatment of

choice.<sup>1,4</sup> Due to their appearances as solid tumours, SBP and SEP are mimicking soft tissue tumours. The SBP most common symptoms at presentation is a bone mass accompanied with pain at the lesion. The SEP usually present as a submucosal lesion with or without involvement of the adjacent bone structures and this lesion must be differentiated from reactive plasmacytosis, immunoblastic lymphoma or plasma cell granuloma.<sup>12</sup> In this report, we presented our experiences of diagnosing and treating solitary plasmacytoma which consist of each case of head and neck SBP and SEP with their characteristic differences, how to exclude both disease with MM and solid tumour, and the differences in treating them.

## 2. Case Presentation

### Case 1: Solitary plasmacytoma of the bone

A 43 years old female was presented to the outpatient clinic with chief complaint multiple solid masses at left frontal. She complained of the growing mass that compressed left eye downward so the left eye vision was blurred. There was no malaise, backpain, history of pathological fracture, loss of weights nor history of gingival bleeding and bruise skin which associated with MM. At physical examination the supraorbital mass was solid and hard in consistency and fixed to bone with 5x4x3 cm in size (Figure 1).



Figure 1. Clinical presentation of case 1: Solid mass at left supraorbital and left parietooccipital.

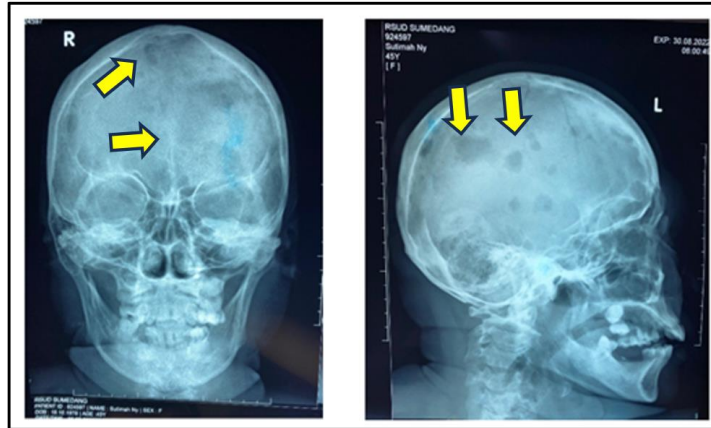


Figure 2. Skull X-Ray: Multiple “punch out” lesions on calvaria (yellow arrow).

The skull X ray showed multiple punch out lesion on calvaria (Figure 2) and the laboratory showed slight anaemia but normal calcium and renal function. The serum protein electrophoresis showed elevated gamma

globulin (45,7%) which indicated for M protein (Figure 3). The bone marrow morphology was performed but the plasma cells count was only slightly elevated (6.0%).

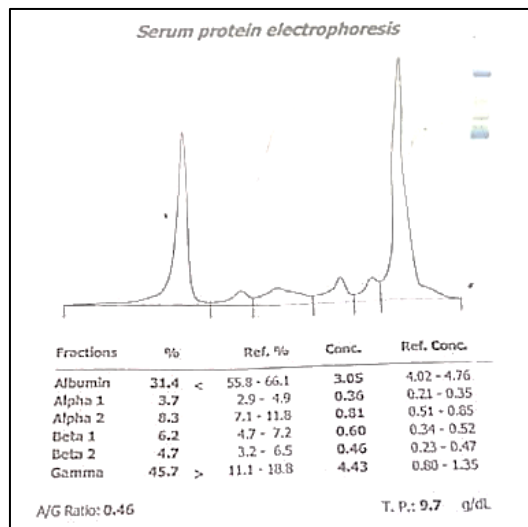


Figure 3. Serum protein electrophoresis showed gamma globulin elevation.

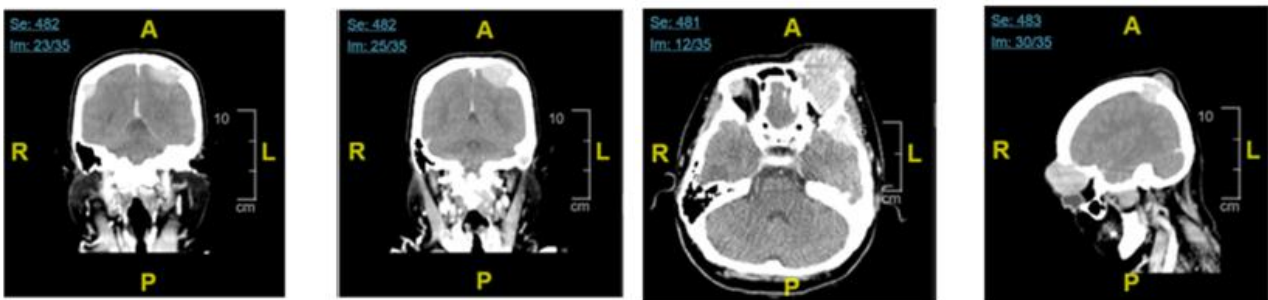


Figure 4. Head Ct scan : multiple punch out lesions.

The histopathology finding showed round to oval monomorphic cells with diffuse eosinophilic cytoplasm, eccentric hyperchromatic nucleus and rarely found mitoses. From H&E staining, the

diagnosis still suspected plasmacytoma. We performed immunohistochemistry and the positive CD45 and CD138 indicating the lesion is plasmacytoma (Figure 5).

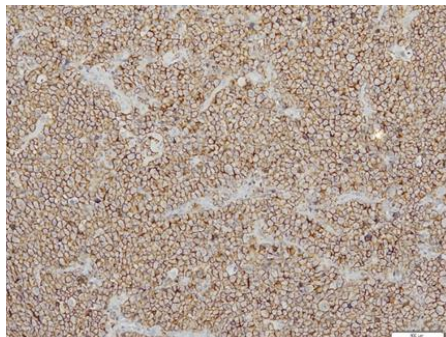


Figure 5. Immunohistochemistry confirmed the diagnosis of plasmacytoma.

Based on the clinical data above, we conclude the final diagnosis is SBP. We treated this patient with External Beam Radiotherapy (EBRT) 40 Gy in 20

fractions of 2 Gy each in five days a week over 4 weeks (Figure 6).

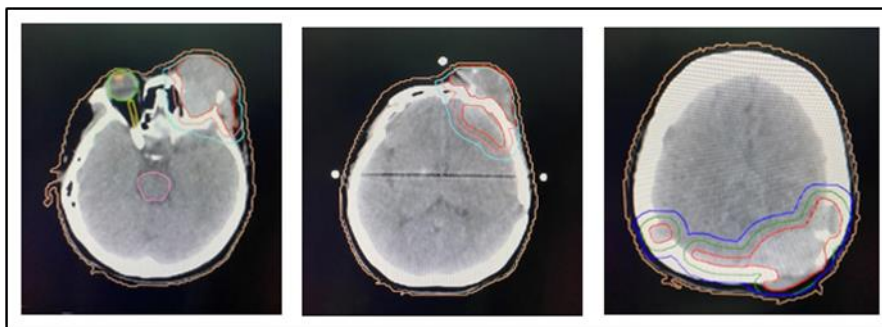


Figure 6. External beam radiotherapy 40Gy in 20 fractions.

One month after radiation therapy, we evaluate the patient, and the mass clinically has shrinkaged both

in clinical appearance and in her head CT scan (Figure 8).



Figure 7. Clinical presentation 1 month after radiation therapy.

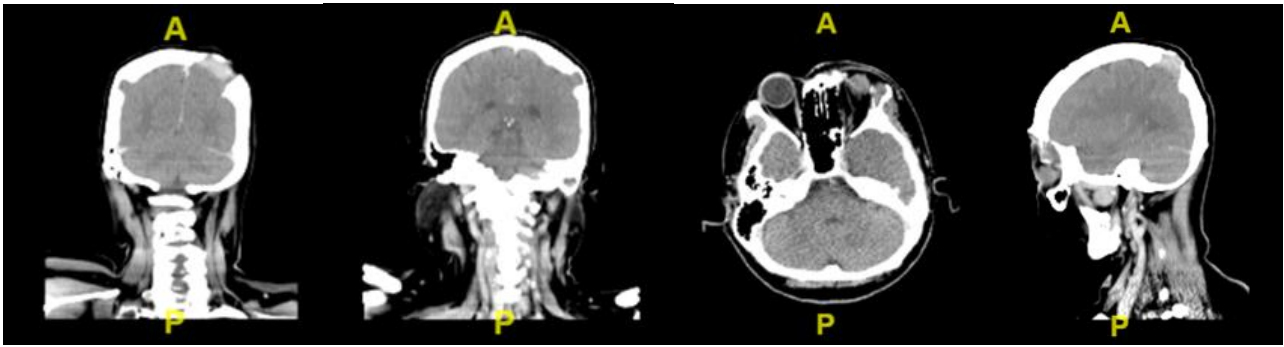


Figure 8. Head CT scan 1 month after radiation showed radiologically improvement.

**Case 2 : Solitary extramedullary plasmacytoma**

A 12 years old girl was presented to the outpatient clinic with chief complaint of a mass at right inferior gingiva for about one year before admission. She complained of gingival bleeding when she brushed her teeth and the mass was growing bigger. There was no other lump in the oral cavity, head nor neck area. There was also no malaise, backpain, history of pathological fracture, nor loss of weights. At physical examination we found a solid submucosal mass at

right inferior gingiva, 2 cm in size, solid in consistency, irregular border, fixed to the mouth floor and mandible, pinkish colour as same as oral mucosa and it pushed the teeth outward (Figure 9).

The laboratory showed slight anaemia but normal calcium and renal function. Serum protein electrophoresis within normal limit, there was no sign of hypergammaglobulinemia (Figure 10). Bone marrow morphology also showed normal limit without plasmacytosis.



Figure 9. Clinical presentation: solid mass at right inferior gingiva.



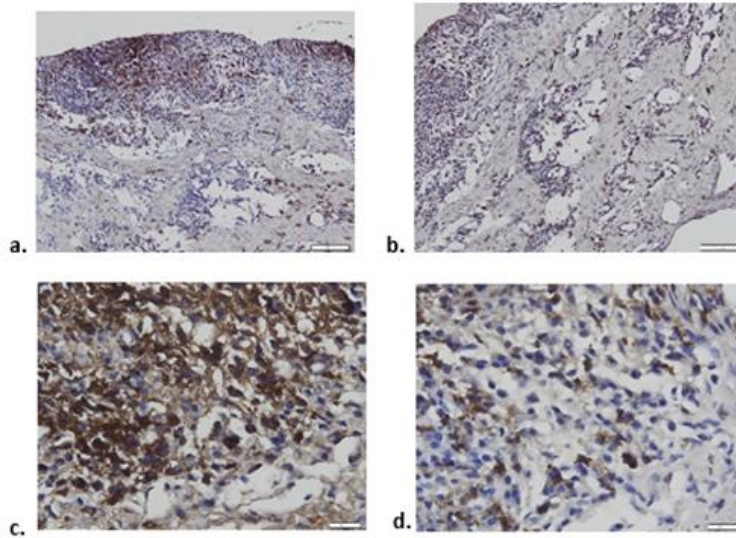


Figure 12. Immunohistochemistry of SEP case: a. CD138 positive, b. Ki67 positive, c.  $\kappa$ -light chain positive, d.  $\lambda$ -light chain negative.

Based on history taking, physical examination, laboratory findings, radiology findings and histopathology assessment, we concluded the final

diagnosis was SEP. We treated this patient with Intensity-Modulated Radiation Therapy (IMRT) 50 Gy in 25 fractions (Figure 13).

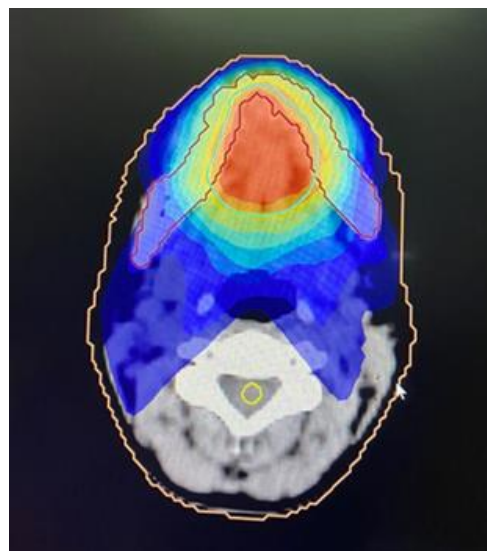


Figure 13. Intensity Modulated Radiotherapy 50 Gy in 25 fractions.

Two months after radiation therapy, the clinical presentation showed very little improvement. Although the mass was still 2x2x1,5 cm in size, it was relatively

mobile to the mouth floor (Figure 14). We performed head CT scan and it showed no radiologically improvement (Figure 15).



Figure 14. Clinical presentation after radiation therapy showed no significant improvement

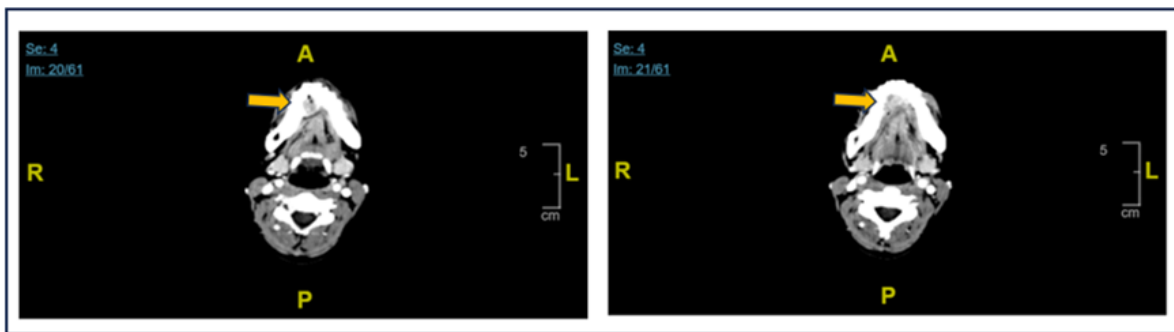


Figure 15. Head CT scan after radiation therapy showed no radiologically improvement.

We performed surgical excision for the tumour. We found a soft tissue mass, solid in consistency, attached to right mandible torus and mouth floor, 2x1x1 cm in size. The mandible was smooth and we found no muscle infiltration on mouth floor. We

performed tumour excision and mouth floor reconstruction with mucosal advancement flap (Figure 16). On 3 months follow up, the wound was completely healing and no signs of tumour recurrence.

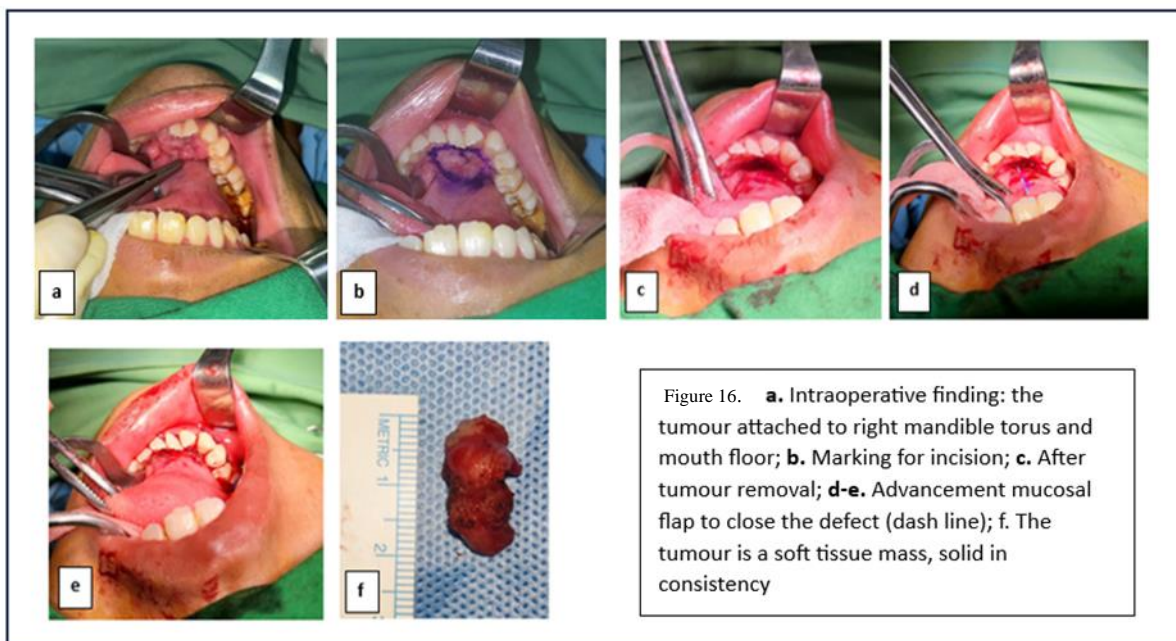


Figure 16. **a.** Intraoperative finding: the tumour attached to right mandible torus and mouth floor; **b.** Marking for incision; **c.** After tumour removal; **d-e.** Advancement mucosal flap to close the defect (dash line); **f.** The tumour is a soft tissue mass, solid in consistency



### 3. Discussion

The incidence of young age is exceedingly rare. Ellington et al reported the age specific incidence rates were lowest among individuals age 20-49 years with incidence rate 0.12/100,000 persons for SBP and 0.04/100,000 persons for SEP.<sup>6</sup> Only few cases of younger than 20 years old patients have been reported and most of them were SBP cases.<sup>13,14</sup> In our case, the SEP patient was 14 years old. Although very rare, Xiaoli et al had reported one patient with SEP whom 15 years old at diagnosis.<sup>15</sup> These cases indicating that the disease can develop in very young age. According to International Myeloma Working Group (IMWG, 2003), the diagnostic criteria of solitary plasmacytoma are biopsy proven solitary lesion of bone or soft tissues with evidence of clonal plasma cells; normal or less than 10% plasma cells in bone marrow at diagnosis; normal skeletal survey and MRI (or CT) of spine and pelvis except for the primary solitary lesion; absence of end organ damage such as hyper calcemia, renal insufficiency, anaemia, and Bone lesion except for primary lesion (CRAB abnormality).<sup>2,3,5</sup> According to Durie and Salmon staging system, SBP is regarded as stage I MM with diagnostic criteria as above.<sup>3</sup> These diagnostic criteria are mandatory to exclude MM from SP because the treatment was very different.

It was mandatory to have history taking, physical examination, complete blood count, serum chemistry for creatinine, calcium, serum LDH, Beta-2 microglobulin, serum quantitative immunoglobulins, serum protein electrophoresis, 24 hours urine for total protein, Bence Jones protein, urine protein electrophoresis, serum free light chain (FLC) assay, bone marrow aspiration and biopsy, skeletal survey [at least radiography, and/or computed tomography (CT), magnetic resonance imaging (MRI) or 18 Fluorodeoxyglucose positron emission tomography (FDG-PET)] to diagnose solitary plasmacytoma.<sup>4,5</sup> Due to limited tools in our hospital, we did not perform all examinations, but we only checked complete blood count, calcium, ureum, creatinine, serum protein electrophoresis, bone marrow aspiration, tissue biopsy and immunohistochemistry and head CT scan which

still could help us to diagnose the lesions. From history taking, both patients did not have another complain except the growing mass and the compression symptoms to adjacent structure. The MM symptoms were asked to exclude the disease: there are no malaise, loss of weights, neuropathy and history of bone fracture in both patients. Bone pain is the most common symptom in MM and affecting 70% of patients and they are also susceptible to bacterial infections, especially pneumonia and pyelonephritis.<sup>1,16</sup> From physical examination, the SBP lesions clinically was mimicking solid tumours while the SEP lesion clinically was confused with granuloma. To confirm the diagnosis, we performed tissue biopsy and immunohistochemistry for both patients. CD45 is expressed on all hematopoietic cells and specific for hematopoietic and lymphatic tumours. CD138 is expressed on plasma cell and plasma cell neoplasms. Ki67 positive result showed the tumour was high proliferation.  $\kappa$ -light chain and  $\lambda$ -light chain was performed to find if the tumour monoclonal or polyclonal plasma cell population. The clonal restriction of one of both chain indicates the monoclonal neoplastic.<sup>17</sup> These histopathology findings were very important to confirm the diagnosis as solitary plasmacytoma. Complete blood count was performed to exclude CRAB abnormality. Both patients only had slight anaemia but the calcium and renal function were normal. The SBP patient had bone lesions on the primary lesions, while the SEP patient did not have. These findings showed there were no CRAB abnormality in both cases.

Serum protein electrophoresis on SBP patient showed elevated gamma globulin, while SEP patient was normal. Diseases that produce an increase gamma globulin level include Hodgkin's disease, malignant lymphoma, chronic lymphocytic leukemia, granulomatous diseases, connective tissue diseases, liver diseases, multiple myeloma, Waldenström's macroglobulinemia, and amyloidosis. Although some diseases could increase the gamma region in serum protein electrophoresis, the spike like peak in gamma globulin region showed monoclonal gammopathy that

are characterized by proliferation of single clone of plasma cells that produce a homogenous M protein. The presence of M protein is commonly used to identify MM and consistently follow by urine protein electrophoresis and immunofixation to confirm the presence of Bence Jones protein (monoclonal free kappa or lambda chain) and this examination need to obtain 24 hour urine.<sup>18,19</sup> We did not perform this examination but as change we performed the immunohistochemistry  $\kappa$  light chain and  $\lambda$  light chain examination to confirm the monoclonal neoplasm. The presence of M protein on SP had been reported but the levels were generally low. It was reported that M protein was detected at 60% SBP and <25% SEP and the persistence of M protein indicating adverse prognostic factors for progressions to MM.<sup>1,2,5</sup> Bone marrow aspiration was performed and the SBP patient showed plasmacytosis < 6.0%, while the SEP patient did not. These findings meet the diagnostic criteria of SP as mentioned above.<sup>2,3,5</sup> On head CT scan, the SBP patient showed punch out lytic lesions on calvaria while the SEP patient showed a solid mass in right inferior gingiva without bone destruction. The punch out lytic lesions on calvaria were similar to MM. These lesions represent osteolytic lesions with little or no osteoblastic activity.<sup>1</sup>

Some study recommended the needs of full skeletal survey, MRI of pelvis and long bones, and PET scanning to diagnose solitary plasmacytoma and exclude MM.<sup>4,5</sup> We did not perform those examinations due to lack of sources, but the two cases still meet the diagnosis criteria of SBP and SEP although both have different clinical features and characteristics. Radiation therapy is the treatment of choice for both plasmacytoma with excellent local control (79%-90%).<sup>10</sup> For SBP of 5 cm or less, a dose of 40 Gy in 20 fractions is recommended. For SBP > 5 cm, a higher dose up to 50 Gy in 25 fractions should be considered. Mendenhall et al reported 31% local failures with dose less than 40 Gy versus 6% incidence of local failure with dose 40 Gy or more, while Frassica et al reported 15,6% incidence of local failure with doses less than 45 Gy and no local failures in patients treated with 45

Gy or more.<sup>3,4,7,16</sup> Our SBP patient was treated with dose 40 Gy in 20 fractions and the result was significant. Radiation therapy for SEP should mind dose and anatomical volume to minimize side effect and maximize local control since the majority SEP occurs in head and neck region.<sup>3</sup> Xiaoli et al recommend dose for SEP is 50 Gy (range 45-55 Gy), while Guideline Working Group of the UK Myeloma Forum (UKMF) recommend same dose as SBP.<sup>5,15</sup> Our SEP patient received IMRT 50 Gy in 25 fractions but clinically only showed very little improvement. Some literature showed that local control and survival rate of radiation alone is better than surgery alone, while other literature showed surgery alone is better than radiation and combined therapy.<sup>15</sup> Since radiation showed local failure, we treat our patient with surgical excision and the result is excellent. Therefore we recommend SP patient which didn't show any improvement with radiotherapy to be treated with surgical excision.

#### 4. Conclusion

The clinical features of head and neck SP often confused with MM and solid tumour. Complete examination from history taking, physical examination, laboratory findings, serum protein electrophoresis, radiology, bone marrow morphology and histopathology including immunohistochemistry examination are very important to determine the correct diagnosis, thus will lead to appropriate treatment planning for the patient.

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