In summary, we described in detail the patient’s characteristics, diagnosis, and treatment processes and tried to explain the possible causes of the disease, hoping to provide the appropriate reference for the peers. In addition, the patient should be followed up to observe the facial development of the maxillofacial region.

REFERENCES


Mandibular Ewing Sarcoma With Chromosomal Translocation t(21;22)(q22;q12)

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Abstract: Ewing sarcoma (ES) is a primary bone malignant neoplasm and is the second most common primary malignancy of the bone found in childhood and adolescence after osteosarcoma. ES has an annual frequency in the population younger than 20 years of approximately 2.9 per million. ES occurs most frequently in the long bones of the extremities and pelvis and only very rarely in the head and neck. ES is an aggressive, highly vascular tumor that is sensitive to radiotherapy and chemotherapy, the current standard treatment consists of a multimodal therapy involving multiagent chemotherapy and radiotherapy, and surgery.1 Therefore, involvement of the jaw and craniofacial bones is scant, at approximately 0.4% to 3% of all ES cases.4,5 Because ES is relatively sensitive to radiotherapy and chemotherapy, the current standard treatment consists of a multimodal therapy involving multiagent chemotherapy, radiotherapy, and surgery.1,3–5 Furthermore, involvement of the jaw and craniofacial bones is scant, at approximately 0.4% to 3% of all ES cases.4,5 Because ES is relatively sensitive to radiotherapy and chemotherapy, the current standard treatment consists of a multimodal therapy involving multiagent chemotherapy, radiotherapy, and surgery.1,3–5

Ewing sarcoma (ES) is a primary bone malignant neoplasm and is the second most common primary malignancy of the bone found in childhood and adolescence after osteosarcoma,1 with an annual frequency in the population younger than 20 years of approximately 2.9 per million.2 ES shows a predilection for the male sex (male-to-female ratio, 1.3–1.5:1).3 It occurs most frequently in the long bones of the extremities and pelvis,2,4,5 and only very rarely in the head and neck.6 ES with an incidence of 1% to 9% of all ES cases.4,5 Furthermore, involvement of the jaw and craniofacial bones is scant, at approximately 0.4% to 3% of all ES cases.4,5 Because ES is relatively sensitive to radiotherapy and chemotherapy, the current standard treatment consists of a multimodal therapy involving multiagent chemotherapy, radiotherapy, and surgery.1,3–5,8 Even when ES appears resectable, neo-adjuvant chemotherapy is performed to eradicate micrometastatic disease and facilitate effective local control with a wide negative margin.9 Such multidisciplinary treatment has dramatically improved survival, increasing the overall 5-year survival rate for ES for all sites from 10% to 50% to 70% over the past 20 years.1,10 Although the prognosis of head and neck ES is similar to or better than that of ES arising in the other anatomic sites such as the extremities,3,5,6 patients with metastatic disease still have poor prognosis.10

Although the cell of origin of ES is not yet known, the molecular genetics of the tumor are better understood.11 It was recently revealed that chromosomal translocation t(11;22)(q24;q12), which fuses the EWS gene on chromosome 22 and the FLI-1 gene on chromosome 11 and encodes a chimeric EWS/FLI-1 protein, occurs in most cases of ES.12 We report here a rare case of mandibular ES in a 10-year-old child with chromosomal translocation t(21;22)(q22;q12) in which the EWS gene is fused with the ERG gene on chromosome 21.

Key Words: Ewing sarcoma, mandible, chromosomal translocation, t(11;22)(q24;q12)

CLINICAL REPORT

A 10-year-old boy with a 6-week history of right mandibular swelling was referred to our department. A lesion in the right mandibular gingiva was hard like bone, and the surface of the mucosa was intact (Fig. 1). There was no paralysis of the right mental nerve. Computed tomography scan showed an expansive bony lesion in the right mandibular body, from the lateral incisor to the first molar, with a sunray appearance on the buccal side (Fig. 2). An incisional biopsy was performed under local anesthesia, and microscopic examination showed sheet formation of small round cells with infiltrative growth of ES in the other anatomic sites such as the extremities,3,5,6 patients with metastatic disease still have poor prognosis.10

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FIGURE 1. Swelling of the right mandibular gingiva and a hard bone-like lesion (arrows), with the surface mucosa intact.

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The tumor cells were strongly positive for CD99 (Figs. 3A, B), slightly positive for synaptophysin (Fig. 3D), and negative for cytokeratin AE1/AE3, S-100, leukocyte common antigen, chromogranin, and CD56. On this basis, we diagnosed it as ES. Whole-body positron emission tomography/computed tomography and bone scintigraphy revealed no metastasis. Pediatric physicians in our hospital planned chemotherapy and decided to apply the highly efficacious St Jude Children’s Research Hospital protocol. The patient underwent induction chemotherapy with ifosfamide, etoposide, cyclophosphamide, and doxorubicin for the first 6 weeks. However, because of a poor response, the patient underwent tumor ablation (segmental mandibulectomy) and reconstruction with a deep inferior epigastric artery perforator flap under general anesthesia. We performed only soft-tissue reconstruction in consideration of the growing mandible and need for postoperative irradiation. Pathological examination revealed a negative margin and numerous active tumor cells, with the sheet formation of small round cells remaining. A molecular genetic study was also performed, and reverse transcription–polymerase chain reaction (RT-PCR) confirmed the presence of reciprocal chromosomal translocation between the EWS gene on chromosome 22 and the ERG gene on chromosome 21; t(21;22)(q22;q12) (Fig. 4). The patient received postoperative radiotherapy (45 Gy; 1.8 Gy/fr) combined with vincristine and actinomycin D chemotherapy. In addition, chemotherapy with ifosfamide, etoposide, cyclophosphamide, and doxorubicin was performed again for 24 weeks. There has been no recurrence or metastasis as of 4.5 years after surgery.

**DISCUSSION**

ES must be differentiated from other small round cell tumors, such as small cell osteosarcoma, embryonal rhabdomyosarcoma, metastatic neuroblastoma, mesenchymal chondrosarcoma, poorly differentiated synovial sarcoma, and malignant lymphoma, yet its diagnosis is difficult owing to its histologic similarity with many malignant tumors. Although differential diagnosis is commonly made from the findings of immunohistochemical staining, cytogenetic study is often also required to differentiate it from other small round cell tumors. For instance, the classic diagnostic problem of distinguishing ES from neuroblastoma and sarcoma is readily resolved by molecular analysis, and genotypic diagnosis might be possible among other small round cell tumors (neuroblastoma, rhabdomyosarcoma, and lymphoma), which have a variety of tumor-specific genetic alterations.

The ES family of tumors (ESFT), defined as a group of small round cell neoplasms of neuroectodermal origin with aggressive behavior, consists of rare bone and soft-tissue tumors characterized by specific genetic alterations. ES family of tumors is composed of ES, extraskeletal ES, and primitive neuroectodermal tumor (PNET) of the bone, soft tissue, and the chest wall (Askin tumor). Immunochemical study is performed for the diagnosis of ES and PNET because the tumor cells are positive for CD99 in most cases, although other round cell tumors may also express this marker. However, as PNETs may exhibit neural differentiation on light microscopy (ie, Homer-Wright rosettes in >20% of tumor tissue), immunohistochemical examination of the expression of markers of neuronal differentiation is performed to distinguish ES from PNET. Although differential diagnosis is commonly made from the findings of immunohistochemical staining, cytogenetic study is often also required to differentiate it from other small round cell tumors. For instance, the classic diagnostic problem of distinguishing ES from neuroblastoma and sarcoma is readily resolved by molecular analysis, and genotypic diagnosis might be possible among other small round cell tumors (neuroblastoma, rhabdomyosarcoma, and lymphoma), which have a variety of tumor-specific genetic alterations.

Both ES and PNET typically have the t(11;22) chromosomal translocation as well as similar histologic features. Molecular genetic studies using fluorescence in situ hybridization (FISH) or RT-PCR are valuable for the evaluation
of undifferentiated small round cell tumors in children, particularly in cases with indeterminate histologic or immunohistochemical features. Therefore, detection of the previously mentioned characteristic translocation by FISH or RT-PCR may allow for the definitive diagnosis of ESFT. ES is characterized by the specific chromosomal translocations of the EWS gene on chromosome 22 being fused to 1 of 5 members of the ETS gene family (ie, FLI-1, ERG, ETV1, FEV, or E1A). A pathogenomic translocation t(11;22)(q24;q12), fusing the EWS gene on chromosome 22 and the FLI-1 gene on chromosome 11, occurs most commonly, in around 83% to 90% of ES cases. ES/FLI-1 has 2 subtypes, types 1 and 2. The second most frequent is EWS/ERG, but it occurs in only 5% to 12.6% of cases. This translocation is t(21;22)(q22;q12), and the present case had the translocation. Also known are rare fusions of the EWS gene, such as EWS/ETV1, EWS/FEV, and EWS/E1A, which may account for perhaps 1% or more of cases or less. Other rare translocations include t(7;22)(p22;q12) with the EWS/ETV1 fusion transcript, t(2;21)(q32;q22) with the EWS/FEV fusion transcript, and t(17;22)(q12;q12) with the EWS/E1A fusion transcript.

Although cytogenetic study is useful for diagnosis of ES, according to previous reports, ES of the jaw has been commonly diagnosed by histologic and immunohistochemical examination. To our knowledge, only a few such cases have been diagnosed by additional FISH or RT-PCR (mandible: 4 cases including present case; maxilla: 1 case). A few authors have commonly reported the translocation (t(11;12)(q24;q12) in ES arising in the jaw, but our case marks the first report of the translocation (t(21;22)(q22;q12)). Makary et al reported that although pathologic diagnosis on preoperative biopsy and resection material of a mandibular lesion in a 17-year-old patient was “sarcoma not otherwise specified,” genetic study by FISH showed a translocation rearrangement in the EWR1 gene at 22q12, thereby confirming a diagnosis of ES. Their case emphasized the importance of the genetic study of undifferentiated (primitive) sarcomas to identify rare morphologic variants of ES.

Because oncologists must consider the issue of chemosensitivity and the potential impact on patient management, there is an increasing trend to accept the diagnosis of ESFT only when substantiated by genetic testing. However, ESFT cannot always be diagnosed by genetic study. In a retrospective analysis of the results of RT-PCR testing and demographic information in patients with known or suspected ESFT, Daghet al found that 58 (76.3%) of 76 patients had translocations (53 with the EWS/FLI-1 fusion transcript and 5 with the EWS/ERG fusion transcript) and that open biopsy or repeat needle biopsy was required to confirm the diagnosis in 5 patients who initially underwent needle biopsy. Indeed, to avoid repeat fine-needle aspiration or core-needle biopsy, it has been recommended that incisional open biopsy be performed to provide adequate tumor samples. Returning to the study of Daghet al, the remaining 18 patients who were translocation-negative, samples from 7 patients were in fact deemed inadequate for RT-PCR testing as a result of inappropriate tissue handling or the presence of necrotic material. In addition, 5 of the 18 patients had their diagnosis revised to neuroblastoma, Wilms tumor, malignant peripheral nerve sheath tumor, or undifferentiated sarcoma on the basis of histologic and immunohistochemical appearance, leaving only 6 samples confirmed as ESFT with no characteristic translocation identified. Although several previous studies found no translocation in 5% or less of tumor samples tested, some of these samples may have been t(7;22), t(17;22), or t(2;22), which have been reported in less than 1% of tumor samples tested. In apparently translocation-negative samples, therefore, close attention should be given to the possibility of an alternative diagnosis, the potential need for nested RT-PCR, and the possibility of an inadequate sample. The diagnosis of ES should be supported by morphologic, immunohistochemical, and molecular genetic study.

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Brief Clinical Studies
Reliability of Preoperative Multidetector Computed Tomography Scan in Patients With Chronic Otitis Media

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Objective: The objectives of this study were to specify the objective criteria of existence of cholesteatoma in chronic otitis media on the preoperative multidetector computed tomography (MDCT) and to evaluate the complications of disease.

Methods: We compared the results of preoperative MDCT scan with intraoperative findings in 71 patients (22 women, 49 men; mean age, 16–73 years) who had mastoidectomy operation between January 2008 and May 2012. Multidetector computed tomography evaluations of temporal bone were performed on a workstation using high-spatial-resolution magnified images with intended angle and plane.

Results: We observed cholesteatoma formation in all patients with scutum erosion (n = 11), dural exposure (n = 6), and lateral semicircular canal fistula (n = 5). Computed tomography revealed these findings with 100% sensitivity. Distortion of ossicular integrity (n = 11) and facial canal dehiscence (n = 5) was significantly higher in cholesteatoma patients. Using the criteria of osteolysis, the sensitivity, specificity, and the accuracy rates of MDCT in detecting cholesteatoma were 71%, 93%, and 88%, respectively. The best diagnostic clue of a cholesteatoma was a mass-like soft tissue located in a retraction pocket in the posterosuperior quadrant of the Shrapnell membrane, causing widening of Prussak space and scutum erosion. Evaluation of computed tomography scan showed nearly 100% sensitivity in detecting tympanic opacification, dural height, dehiscence of lateral semicircular canal, tegmen tympani erosion, and deformation of malleo-incudal articulation. However, its contribution to detecting minor ossicular erosion, facial canal dehiscence, and incudostapedial joint evaluation was limited.

Conclusions: Preoperative assessment of chronic otitis media via MDCT with intended angle and plane produces important guidance to understand the extent of disease and to prevent possible intraoperative complications.

Key Words: Computed tomography, otitis media, cholesteatoma, temporal bone

Chronic otitis media is the term used to describe signs, symptoms, and physical findings that result from long-term damage to the middle ear from infection and inflammation. Cases can be categorized as 1 of 2 subtypes: chronic otitis media with cholesteatoma or chronic mucosal disease. Because of the high risk of intracranial and extracranial complications, surgical treatment is mandatory in the cholesteatoma group. Although osteolysis is not expected in cases of chronic otitis media without cholesteatoma, because of the possibility of auditive sequelae, surgical treatment may warrant improvement in hearing in several cases.1,2 Therefore, establishing a differential diagnosis between the 2 subtypes is critical.

Although accurate otomicroscopic examination can diagnose cholesteatoma, radiological imaging is generally required to evaluate the nature and extension of the disease and anatomic variations. At present, the most accurate technique to study the temporal bone (T-bone) is multidetector computed tomography (MDCT). State-of-the-art computed tomography (CT) scanners not only provide high-spatial-resolution images, but also offer the possibility of evaluating small structures, particularly those requiring microsurgery, on the monitor and creating reformatted images with intended angle and plane. A combination of these analytical strategies improves spatial, temporal, and contrast resolutions of the images and thus significantly increases the diagnostic accuracy of the examination.3 Even then, the radiologist must be careful regarding the possible extension of the disease to the critical areas of tympanoantral cavity to facilitate the best surgical treatment plan.4 Furthermore, whenever a complicated disease is suspected, it is invaluable to identify these complications, which can be life-threatening.1 Although T-bone CT scan can display more valuable information because of the improved imaging technology, there is still no general consensus regarding its usefulness on the preoperative evaluation of chronic otitis media.1,5–7

The objectives of this study were to determine the results and limits of preoperative MDCT scanning in chronic otitis media and to evaluate the clinical value of this imaging technique in determining the nature and complications of the disease.

MATERIALS AND METHODS

This retrospective study was approved by our institutional review board, and written informed consent was obtained from all patients. We compared the preoperative T-bone CT scans of 71 patients (22 women, 49 men; mean age, 34 years) with chronic otitis media, with intraoperative findings between January 2008 and May 2012. No patient had previous ear surgery.

Preoperative T-bone CT (Philips Brilliance ICT 256; Medical Systems, Best, the Netherlands) was performed without the use of intravenous contrast material (except for 2 patients). The CT acquisition parameters consisted of a 251-mAs tube current, 120 kV, 64 × 0.625 detector collimation, 0.5-second rotation time, table speed of 1 mm per rotation (pitch, 0.391), 0.67-mm slice thickness, 4.9-second scan time, field of view of 294, and matrix of 1024 × 1024. A power injector was used with 2 patients to inject 100 mL of nonionic contrast material (Ultravist 370; Schering, Berlin,