REVIEW ARTICLE

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Intraosseous schwannoma of upper limb – review

Katarzyna Kopcik[1,A-D] ✉, **Agnieszka Koberling**[1,B-D], **Franciszek Rzymkowski**[2,E-F], **Magda Bichalska-Lach**[1,E-F]

[1] *Department of Surgical Nursing and Propaedeutics of Surgery, Faculty of Health Sciences, Medical University of Silesia, Katowice, Poland*
[2] *Departament of Radiology, Czerniakowski Hospital, Poland*
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Abstract

Introduction and Objective. Intraosseous schwannoma is a neoplasm originating from Schwann cells of nerve sheath. It is mostly located in mandible, maxilla or sacrum, but there are cases of upper limb location. The aim of the review is to summarize current knowledge about intraosseous schwannomas located in the upper extremity.

Review Methods. The review is based on scientific publications available in PubMed, Wiley Library, Embase, Web of Science, Google Scholar and NCBI databases. After evaluation of articles' abstracts, papers were selected and analyzed, considering the references cited.

Brief description of the state of knowledge. Intraosseous schwannoma of the upper limb is relatively rare, but there are cases in literature involving the ulna, radius, humerus, hamate, metacarpals and phalanxes. Diagnostic methods include classic radiology, computed tomography, bone scan and magnetic resonance imaging. Final diagnosis is made based on histopathological image and microscopic evaluation. Treatment methods are surgical excision, curettage and bone allografting. Recurrence is typically connected with incomplete resection. In cases of total excision, recurrence is rare.

Summary. Intraosseous schwannoma may lead to pathological fracture and it is important to take this into consideration during the diagnostic process. Treatment of choice is complete removal of the lesion, in some patients followed by bone grafting or cementing. Recurrence rates are lo, if the excision is total. Due to the rare localization in the upper limb, research on intraosseous schwannoma in this area needs to be extended.

Key words

neurology, upper extremity, orthopedics, neurilemmoma

INTRODUCTION

Schwannomas are a common benign soft tissue tumor that affect peripheral nerves. It originates from the Schwann cells of nerve sheaths. Intraosseous schwannoma is significantly more rare and most commonly localized in the mandible, maxilla and sacrum. Location in the limbs is infrequent. The tumour may be asymptomatical, or may cause pain or paresthesia. Diagnostic methods include classic radiology, computed tomography, magnetic resonance imaging and histological examination. Treatment is total resection, curettage or bone allografting. Recurrence is rare, and if occurring – tends to be connected with incomplete excision. The aim of the review is to summarize available knowledge about intraosseous schwannomas located in the upper extremity.

MATERIALS AND METHOD

The review is based on scientific publications available in PubMed, Wiley Library, Embase, Web of Science, Google Scholar and NCBI databases. After initial evaluation of articles' titles and abstracts, papers were selected and analyzed, considering the references cited.

Background. Schwannoma, also known as neurilemmoma, is a most common benign tumour of the peripheral nervous system and makes up to 10% of all soft tissue tumours. It originates from the Schwann cells which form the nerve sheats. The function of these cells is to myelinate peripheral nerves [1, 2]. It is believed that neoplasmic transformation of Schwann cells is a result of mutations in the Nf2 tumour supressor gene, which lead to its function loss, but there are also studies suggesting that tumour microenvironment may be also involved [3]. Schwannoma is encapsulated and frequently located in soft tissues, mostly of the head and neck area, but in some cases the neoplasm can be found in the extremities or chest [1, 2, 4]. Approximately 25% of schwannomas are located in head and neck area [4]. Intraosseous schwannoma is relatively rare, and its incidence is estimated for about 0.2% of primary bone tumours [2]. Schwannomas usually appear as sporadic, but some cases are related with neurofibromatosis type 2 (NF2), Carney complex or schwannomatosis [5–7]. Connection to NF2 is taken under consideration especially in cases of peripheral or multiple schwannomas [7]. There are suggestions that neoplasm may be connected with chromosomal aberrations, mostly regarding chromosome 22. [7,8]. Rarely, schwannomas transform into malignant peripheral nerve sheath tumours, and up to 50% of malignancy events are connected with neurofibromatosis [1, 5].

✉ Address for correspondence: Katarzyna Kopcik, Department of Surgical Nursing and Propaedeutics of Surgery, Faculty of Health Sciences in Katowice, Medical University of Silesia, Żeromskiego 7, 41-902 Bytom, Poland
E-mail: kopcik.katarzyna1@gmail.com

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Schwannoma is a slow growing tumour that is often asymptomatical, especially intraosseous neoplasm [9]. Symptoms may be present in 25% of cases, and in intraosseous tumours cause pain rather than sensory or motor impairment. In some cases, tingling or paresthesia may be present [5, 10–12]. Schwannomas do not invade the nerve fibres and symptoms are due to nerve compression, with a positive correlation established between the size of the lesion and neurological deficits. The late onset and non-specific character of symptoms, such as neuropathic pain, can delay proper diagnosis [1, 13, 14], and it can occur at any age, but it is usually seen between 40 – 60 years old. It is equally present in both genders, but some papers show slight predilection towards females [2, 15]. In peripheral schwannomas there is no gender predominance [7].

The tumour tends to be located eccentrically towards the nerve from which it originates in contrast to neurofibromas, which are placed more centrally to the nerve [5]. Neoplasm tends to affect sensory nerves more frequently [16]. Schwannoma is usually well defined, surrounded by its capsule and mobile tumour. It tends to occur solitarily (up to 90% of cases), although multiple neoplasms have been reported (approximately 9–15% of cases) [1, 9, 17].

Intraosseous schwannoma usually originates from intraosseous nerves, although invasion of bone occurs in one of three mechanisms [5, 16]:
– being located in the nutrient canal;
– intramedullary location;
– extraosseous location with intraosseous invasion.

Intraosseous nerves tend not to be myelinated, which may be connected to how rarely intraosseous schwannomas localize in the limbs. The intraosseous location is characteristic for the mandible, maxilla or sacrum, but can be present in any bone of the skeleton. There are case reports of intraosseous neurilemmomas located in the spine. Neurilemmomas may be present in long bones, and it is suggested that in such cases the tumours originate from the nutrient canals. [5, 10, 15, 16, 18–21].

Diagnostic methods. According to the literature, in cases of intraosseous schwannomas, ultrasound examination, classic radiology, magnetic resonance imaging and bone scintigraphy are used, and the final diagnosis based on microscopic evaluation.

In ultrasonography, neurilemmomas appear as homogenous, hypoechoic masses with defined borders. In some cases it is possible to visualize a connection to the nerve of origin [9].

The classic radiological image of intraosseous neurilemmoma reveals well-defined osteolytic lesions with sclerotic margins, cortical expansion, trabeculation or multiloculation, lobulated contours with no central calcification. The image is not specific and it is vital to differentiate diagnosis with bone cyst, aneurysmal bone cyst, giant cell tumour, fibroma or enchondroma, which can be challenging [16, 21, 22].

Computed tomography (CT) is a tool that may suggest diagnosis, as it reveals connection of the tumour and soft tissue [16]. Typical factors of benign tumours are also present – thin rim of transmission cells and absence of periosteal reaction. It is important to remember that these signs are not specific [5].

Magnetic resonance imaging (MRI) reveals masses growing out of its original nerve, in most cases eccentrically. It may show the relations between tumour and its surroundings [17]. Schwannomas appear as hypointense or isointense on T1-weighted scans, and hyperintense and heterogeneous on T2 scans [5, 15]. They tend to enhance after contrast application. Differentiating neurilemmoma and malignant peripheral nerve tumour is a great challenge. Malignancy often appears as size greater than 5 cm and infiltrative borders of the neoplasm [5].

Final diagnosis is made after histological evaluation. Material is collected during surgical excision. Typical histological pictures of both soft tissue and intraosseous schwannoma include Antoni A and Antoni B regions. Antoni A pattern is constituted by spindle cells with long, wavy nuclei in bundles or fascicles, and its appearance is more organized. Antoni B patterns tend to be less organized with more myxoid and less packed tissue [1, 23]. In some cases, nuclei can form parallel rows with a pink fibrillar structure that forms 'nuclear palisading', also described as Verocay bodies, named after Jose Verocay who described pathological image of schwannoma cells for the first time [23]. Sometimes, neoplasm may appear with images of hyalinized vascular structures with thick walls [2]. Characteristic for neurilemmomas is also immunoreactivity for protein S-100 and SOX-10, and this knowledge is helpful in differential diagnostics. Other characteristic staining (negative) for smooth muscle marker – desmin, gastrointestinal stomach marker DOG-1, cytokeratin AE1/AE3 and myoepithelial marker p63, respectively, are used to rule out histological differential diagnoses [10]. Pathological variations are ancient, cellular, epithelioid, plexiform or melanotic schwannoma [1, 5, 16, 22].

Management. Intraosseous schwannoma has a positive prognosis with malignant transformation and recurrence being unlikely [2, 16]. Treatment of choice is complete resection or curettage of the neurilemmoma with bone grafting [16]. Iliac crest autograft is used most frequently, but this is connected with a risk of complications, from a minor complication, such as haematoma or mild infection, to major, like severe infection, destruction of vascular structures, iliac fracture, or even abdominal hernia. Another limitation for bone grafting is the difficulty to grow a graft from osteoporotic bone, which may affect older patients. Drumond et al. described a method of grafting using cementation, which can be used in this group of patients. Cement can increase the stability and mechanical strength of destructed bone, and can be used not only in elderly patients, but also in cases of pathological fracture or wide bone resections. Cement allows early detection of recurrence, as revealing a radiolucent lesion within the cement or in the border between it and the bone, may be suggestive of regrowth of a tumour. Another advantage is hyperthermic reaction caused by cement polymerization, which may cause destruction of remaining neoplastic cells [22]; however, treatment including bone-grafting is preferred over methods using bone cement [20].

If excision is total, recurrence is infrequent. Regular follow-up seems to be necessary, as recurrence was reported in cases of incomplete resection, with a recurrence rate of 16% [2, 22]. In the case of pathological fracture, management should include its fixation [10]. It is important to remember

that postoperative complications may occur, including sensory and motor malfunctions, and nerves with major motor function tend to have a greater risk of neurological deficits [24].

Selected cases of intraosseous schwannoma in upper limb. Schwannomas located in peripheral nerves is a common tumour with the majority located in the flexor parts of extremities [7]. A retrospective study by Sayed et al. in 2022, describing solitary schwannomas in extremities, showed that nerves affected in the upper limb may be median (the most common), ulnar, radial, collateral, suprascapular, musculocutaneous and medial cutaneous of the forearm. In some cases, brachial plexus may be affected [25–27]. The ulnar nerve tends to be the most common location [9]. The upper limb is affected in approximately 19% of cases [6, 8]. Intraosseous schwannoma of limbs is rare, although there are case studies in literature describing this type of neoplasm in the upper limb.

Typical presentation was pain with no history of trauma with preserved range of motion. Ultrasonography, classic radiology, CT and MRI, are used as basic diagnostic methods, followed by biopsy. Treatment was surgical, in some cases with bone grafting, with a low rate of recurrence.

a) **Ulna.** Kito et al. reported a case of an intraosseous neurilemmoma in a 21-year-old woman. The tumour was located in the left proximal ulna and was the very first case describing this kind of neoplasm in this location. The patient reported pain of left elbow one month prior to examination, with no trauma history or skin destruction, and with full range of motion. CT and MRI scans were administered and open biopsy was performed. Histological evaluation revealed that most of the material showed Antoni A pattern. Mitosis or necrosis were not present, but there was a strong reactiveness of S-100 protein. After diagnosing the tumour as intraosseous schwannoma, tissue of the neoplasm was completely resected. After 3.5-years follow-up, the patient did not show any signs of recurrence, neither clinically nor radiologically [16].

Another case of intraosseous schwannoma of the proximal ulna was described by Lim et al. The patient was a 77-year-old female who collapsed, and the tumour led to pathological ulnar fracture. The patient reported to hospital with pain in the right elbow, with no skin damage and normal vascular and neurological state. Material collected during open biopsy presented spindle cells organized in fascicles with palisading. Cells were S-100 positive. Management was surgical excision with curettage, but in this case, obtaining bone grafts was challenging due to osteoporosis. Bone loss was completed with β-tricalcium phosphate and hydroxyapatite, and augmented with bone cement. Right elbow was immobilized for 2 weeks post-surgically, and a control X-ray scan presented positive results of the procedure. After 3-year follow-up, the patient did not present any manifestations of recurrence. Final diagnosis for this patient was ancient intraosseous schwannoma, and this case may be the first for this histological image, which was managed with the bone-cementing method [22].

The next case describing intraosseous schwannoma in the area of the elbow joint was reported by Suzuki et al. An 87-year-old female experienced a fast-growing mass on the medial side of her left elbow, with full range of motion and muscular strength of the limb. X-ray scan presented a well-circumscribed structure in the proximal ulna connected with a fracture. MRI scans were typical for schwannoma. Open biopsy was performed and examination of tissue obtained was evaluated as probable benign schwannoma with spindle cells. Treatment in this case was surgical removal of the structure, followed by curettage, and the deficit was filled with hydroxyapatite granulate. The tumour was pathologically evalued, which revealed strong activity of S-100 protein. The final diagnosis was intraosseous schwannoma. One year later, the patient had no symptoms of recurrence [21].

b) **Humerus.** Huajun et al. described a 55-year-old female with right shoulder pain, which had present for a year previously, and had increased after tripping and collapsing. No history of other previous trauma or surgery was reported. She experienced limited range of motion. X-ray scan of the shoulder exposed osteolytic lesion with marked margins, with no presence of periosteal reaction. CT confirmed homogenous bone lesions, well-defined and with a narrowed cortical layer, and revealed a fracture within the proximal part of the humerus. MRI scan showed a typical image of the structure that was isointensive towards skeletal muscles in T1-weighted images, and hyperintense in T2-weighted image. The structure involved the anterior, medial and posterior facets of the proximal part of the humerus. Shoulder joint remained normal. Histological image of material obtained in open biopsy confirmed the diagnosis of schwannoma, with the presence of S-100, SOX-10, CD68 proteins. After resection biopsy, bone grafting was performed and fixation of the pathological fracture. After 6 months, a classic radiology scan revealed no signs of tumour recurrence [10].

Hansra et al. presented a case of intraosseous schwannoma of the distal part of the humerus in a 17-year-old female who reported a painless tumour located in the arm. The patient had no history of trauma or surgical treatment. Radiological examination presented a typical picture for intraosseous schwannoma, except for MRI scan, which did not reveal any enhancement in the mass after administering a contrast agent. Fine needle biopsy under ultrasound guide was performed, and pathological evaluation revealed spindle cells with no malignancy factors, but with presence of S-100 protein. This examination let physicians to form a final diagnosis of intraosseous schwannoma, but the possibility of neurofibroma was not excluded. A second MRI scan was performed 3 months later. This case was not typical, because in the first MRI scan, extraosseous component did not show enhancement after contrast application, but in the second examination this structure did appear as enhanced. This may have been an effect of fine-needle biopsy, after destructing pseudocapsule of the neoplasm, leading to a decrease of pressure inside the tumour. Surgery was performed 4.5 months after initial diagnostics [5].

c) **Radius.** Sun et al. reported the case of a 29-year-old male with a painless mass located on the radial side of the right forearm, which had been present for 4 months. Classical radiology, CT and MRI suggested radial schwannoma, which was confirmed with biopsy, as Antoni A and B regions and Verocay bodies were present. Physicians

performed biopsy followed by surgical removal of the tumour, with bone grafting. Histological evaluation revealed high activity of S-100 and SOX10 proteins. After 12 months follow-up there were no signs of recurrence in clinical examination and radiological scans [28].

Intraosseous schwannoma in the radius in a 19-year-old female was also presented by Bagci et al. The patient had a history of radial fracture. In this case, bone scintigraphy with Tc-99m was performed which revealed increased activity in the radial area. Initially recommended differential diagnosis included Ewing sarcoma, osteosarcoma and fibrous dysplasia. The first histopathological evaluation was described as 'healing pathologic fracture', but material collected after curettage was evaluated as primary intraosseous schwannoma, due to its typical microscopic presentation, with no recurrence after a few years follow-up [29].

d) **Hamate.** Schwannoma in an unusual location was reported by Gurkan et al. A 34-year-old female with a 2 year history of wrist pain, presented with a firm, round mass on the dorsal side of the right wrist. Range of motion was almost full, with no signs of erythema or warming, but with slight swelling. X-ray scan showed a lytic bone lesion with sclerotic margins, multiloculated, with no signs of central calcification, located in the hamate bone. The cortical layer of the bone on its dorsal side was destroyed, but showed no periosteal reaction. CT scan confirmed a well- defined mass with sclerotic margins, with a narrow transition rim. MRI scan presented destruction of the cortical layer of the dorsal aspect of the hamate, and extraosseous extension of the soft tissue, on the dorsal side of the hand. Needle biopsy was performed, and pathological examination revealed spindle cells containing S-100 protein. The next step was a surgical resection. After curettage of the neoplasm, autograft bone harvested from the iliac crest was implemented. No adjuvant therapy was performed. The lobular tumour underwent histological examination, which presented domination of Antoni A regions, Verocay bodies and nuclei palisading. Final diagnosis was plexiform schwannoma of the bone. Seven months later, during a follow-up examination, the patient did not show any symptoms of recurrence [30].

Other locations of intraosseous neurilemmoma in the hand have been described in metacarpal bones and phalanxes [31–34]. Metacarpal schwannomas presented a typical radiological and histological picture, and treatment was based on curettage followed by bone grafting.

Selected cases of intraosseous schwannomas are summarized in Table 1 [5, 10, 16, 22, 28, 29, 35].

Among 8 cases of intraosseous schwannoma located in the upper extremity, 7 patients were female. In all cases treatment was surgical, based on resection and curettage, in some cases followed by bone grafting or bone cementing. Recurrence rate was low; in all cases there were no signs of recurrence after follow-up. In one case recurrence state was not mentioned.

Table 1. Selected cases of intraosseous schwannoma in upper limb

Study	Location	Gender	Treatment	Recurrence
Kito et al.	Ulna	F	Excision	No
Lim et al.	Ulna	F	Excision and curettage, bone cement	No
Suzuki et al.	Ulna	F	Excision with curettage and hydroxyapatite filling	No
Huajun et al.	Humerus	F	Excision with bone grafting and fracture fixation	No
Hansra et al.	Humerus	F	Excision with curettage, bone grafting and synthetic putty	Not stated
Sun et al.	Radius	M	Excision with bone grafting	No
Bagci et al.	Radius	F	Curettage with bone grafting	No
Gurkan et al.	Hamate	F	Excision with curettage and bone grafting	No

SUMMARY

Intraosseous schwannoma usually occurs in the mandible, maxilla or sacral bone, and rarely occurs in the limbs. In literature one can find case reports of this type of benign tumour in the upper limb, involving the ulna, radius, humerus, hamate, metacarpals and phalanxes. The tumour may lead to pathological fracture. The most widely used evaluation methods are classic radiology, ultrasonography, computed tomography and magnetic resonance. Bone scan can be also administered. Final diagnosis is made after histological evaluation of the tumour tissue, and treatment of choice is complete removal of the lesion, in some patients followed by bone grafting or cementing. Recurrence rates are low in cases where excision is total. Due to the rare localization in the upper limb, research on intraosseous schwannoma in this area needs to be extended.

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