Abstract.—I-131 MIBG scintigraphy is routinely used in the diagnosis of neuroendocrine tumours with high specificity. The radiopharmaceutical is taken up via uptake mechanism and actively transported into storage vesicles. The organs with dense sympathetic innervation such as salivary glands, heart, lachrymal glands, spleen and rarely adrenal medulla are normally visualized with I-131 MIBG. Asymmetrical salivary gland uptake is important in a patient with suspected neuroendocrine tumours. Absence of radioactivity may be a result of sympathetic denervation or tumor. Bilateral radioactivity absence is observed usually due to drugs or radiopharmaceutical storage conditions. Detailed examination of cervical region is crucial for localization of neuroendocrine tumours. Therefore, possible false positives should be kept in mind.

KEY WORDS: salivary gland, I-131 MIBG scintigraphy, neuroendocrine tumours.

INTRODUCTION
I-131 MIBG scintigraphy is a well-known radiotracer which is widely used in the evaluation of neuroendocrine tumours such as neuroblastoma, pheochromocytoma. Although, lower sensitivities have been reported, it has a role in the evaluation of other tumours such as carcinoid tumours, chemodec- toma, schwannomas, and Merkel cell tumours, APU- Domas of unknown origin. I-131 MIBG enters neuroendocrine tissues by means of uptake-I mechanism. From the cytoplasm there may be further active transport and storage into membrane bound storage granules. Stored tracer is discharged when cell membrane depolarization leads to a calcium influx, followed by exocytose of storage vesicle contents. Biodistribution of I-131 MIBG includes organs with dense sympathetic innervations such as salivary glands, heart, lachrymal glands, spleen and rarely adrenal medulla. Excretory sites are also visualized such as kidneys, bladder, and intestine. Also, metabolic uptake is observed in liver. As mentioned salivary glands show bilateral symmetric uptake of I-131 MIBG. In this article the authors describe two cases which showed different I-131 MIBG uptake patterns in salivary glands. The mechanisms of these two different uptake patterns and other reasons that may show similar patterns are listed.

CASE REPORTS
Case 1
A 32-year-old woman had a history of an operation from her left neck because of a palpable mass two years ago. After the operation, she has xerophthalmia of the left eye and anhydrosis of the left half of the face. She was diagnosed with Horner syndrome. Two months ago she was admitted to the hospital with palpitation, flushing and hypertension. She was...
hospitalized with the prediagnosis of pheochromocytoma. Her neck and abdominal computerized tomographies were reported to be normal. On the urine analysis metanephrin, normetanephrin, vanillic acid levels were normal. Blood epinephrine levels were found to be high. Therefore, the patient was referred to Nuclear Medicine Department with the suspicion of paraganglioma for I-131 MIBG scan.

I-131 MIBG (37MBq) was administered by slow intravenous injection, after the patient used lugol solution per oral for two days. The patient continued to take lugol solution for five more days. Twenty four hours after the injection of the radiopharmaceutical, wholebody scanning was performed by ADAC Genesis (USA) gamma camera with high energy collimation.

The I-131 MIBG distribution was normal on wholebody imaging except for salivary glands. I-131 MIBG uptake was absent in the left parotid gland and left submandibular gland while the uptake was normal on the right side of the face (fig. 1).

A salivary gland scintigraphy with Tc-99m pertechnetate was performed to assess the functional status of the salivary glands. The scintigraphy revealed bilateral normal concentration and excretion after stimulation with lemon juice (fig. 2).

**Case 2**

A 6-year-old boy with abdominal mass was admitted to hospital. The mass was also discovered in physical examination over the right upper abdomen. The abdominal CT revealed a suprarenal mass containing focal calcification with dimensions of $35 \times 32 \times 15$ mm. Excisional biopsy was carried out and the patient was diagnosed as neuroblastoma. Bone marrow biopsy revealed rosette formation and therefore, the patient was staged as stage 4 neuroblastoma.

The patient was referred to Nuclear Medicine Department for I-131 MIBG scintigraphy. The patient was prescribed lugol solution and ordered to take the solution per orally before coming to the department for I-131 MIBG administration. On the day of injection, it was learned that the patient had not taken the prescribed drug. Therefore, I-131 MIBG administration was postponed for 24 hours. The patient received lugol solution and 15 MBq I-131 MIBG was injected with slow infusion in the following day. The 24-hour wholebody scan showed decreased uptake in salivary glands (fig. 3).

**DISCUSSION**

Imaging tumours of neuroendocrine origin (pheochromocytoma, neuroblastoma, paraganglioma, carcinoid type tumours) with I-131 MIBG is possible using active transport mechanism: uptake-I mechanism, present on the cell membrane which is sodium-dependent, saturable, high-affinity, low-capacity uptake mechanism. Uptake-I system predominates when the concentration of MIBG is low; uptake by
diffusion (Type II) occurs at higher concentrations. Iodine 131 or I-123 labelled MIBG is structurally similar to guanethidine, a precursor of epinephrine. Neuroendocrine tumour cells use MIBG as a substrate for synthesis of hormones, epinephrine. The tumour cells using active transport into the cytoplasm and stored into membrane bound vesicles take up MIBG. MIBG concentration in the tumour increases by the time, conversion of the MIBG to epinephrine doesn’t take place. Normal I-131 MIBG distribution includes salivary glands, heart, lachrymal land, spleen, which have rich sympathetic innervation and the excretory sites (kidneys, bladder, intestine and liver). Rarely faint visualization of adrenal medulla is observed. Stored tracer is discharged when cell membrane depolarization leads to a calcium influx, followed by exocytose of storage vesicle contents.

Horner syndrome usually results from the interruption of descending autonomic fibbers in the brain stem or cervical spinal cord and the lesions involving either preganglionic or postganglionic sympathetic fibbers of superior cervical ganglion. Brain stem stroke, carotid dissection during head and neck surgery, neoplasm impinging upon the sympathetic chain are causes of Horner syndrome while most of the cases are idiopathic. The patients may present with anhydrosis, pseudoptosis, enophthalmos, and meiosis.

Volkan B et al. Patterns of salivary gland uptake in I-131 MIBG scintigraphy

Fig. 2.—(A) Salivary gland scintigraphy of the 52 years old woman. Both parotid and submandibular glands had normal concentration function. Lemon juice was given on the 20th minute p.o. Normal excretion functions of the salivary glands were demonstrated. (B) Lateral views showing normal concentration of the salivary glands.

Fig. 3.—A 6-year-old boy with abdominal mass. The 24-hour whole-body I-131 MIBG scan showed decreased uptake of the salivary glands.
Our patient in the first case was diagnosed with Horner syndrome. I-131 MIBG uptake is directly related to intact sympathetic neurons. In our opinion, in this case, asymmetrical MIBG uptake of salivary glands was due to absent sympathetic innervation on the left side of the face, secondary to the operation the patient had before. Such presentation is not uncommon in head and neck neuroblastomas of the childhood. The salivary gland scintigraphy revealed normal function of bilateral parotids and submandibular glands, which supports this hypothesis.

Asymmetrical MIBG uptake can be seen in patients with chemodectomas and may be mistaken as physiologic asymmetry of salivary glands. Other possible causes that may present with asymmetrical MIBG uptake of salivary glands are listed in table 1.

In the second case, bilateral decreased uptake of salivary glands may be secondary to dissociation of the pharmaceutical due to improper storage conditions. In our clinic MIBG-131-D kit by CIS bio-international (France) is used. The vial should be kept frozen in –18 °C until injection. The expiry date for that product had been thawed more than once as stated in the package inserts. The injection of MIBG to the second case was delayed for 24 hours after the product had been thawed and the solution was not re-frozen and kept at room temperature for one day. Another patient whom MIBG is injected on the day of arrival revealed bilateral normal salivary uptake.

In conclusion, in cases of unilateral or bilateral absent I-131 MIBG uptake of the salivary glands, Horner Syndrome and storage of I-131 MIBG under improper conditions, respectively should be considered and investigated among other causes.

REFERENCES


Table 1

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<thead>
<tr>
<th>CAUSES OF ASYMMETRICAL I-131 MIBG UPTAKE OF SALIVARY GLANDS</th>
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<tbody>
<tr>
<td>1. Cervical neuroblastoma</td>
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<td>2. Pheochromocytoma</td>
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<td>3. Surgical excision, chemical denervation</td>
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<td>4. Chemodectoma</td>
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<td>5. Agensis, hypoplasia</td>
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<td>6. Inflammation</td>
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Table 2

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<tr>
<th>CAUSES OF BILATERAL ABSENT I-131 MIBG UPTAKE OF SALIVARY GLANDS</th>
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<td>1. Drugs</td>
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<td>2. Storage of I-131 MIBG under improper conditions</td>
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<td>3. Idiopathic sympathetic autonomic neuropathy</td>
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<td>4. Previous administration of unlabelled (cold) I-131 MIBG</td>
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