Immature gastric teratoma in an infant: a case report and review of the literatures

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Key Clinical Message
Immature gastric teratoma is an uncommon germ cell tumor of the stomach. We report a rare case of immature gastric teratoma in an infant with down syndrome with clinically presenting with hematemesis and severe anemia. Complete surgical resection remains the cornerstone of treatment.

Keywords
Down syndrome, extramedullary hematopoiesis, immature teratoma, stomach

Introduction
Teratoma is defined as germ cell tumor composed of tissues derived from ectoderm, endoderm, and mesoderm and has been described in various locations, including the gonad, intracranium, anterior mediastinum, retroperitoneum, and sacrococcygeal region. The alimentary tract accounts for <1% of all teratomas [1]. Gastric teratoma was first reported by Eusterman and Sentry in 1922 [2]. Gastric teratomas are considered to be benign nature; however, immature teratomas appear to be more aggressive and have malignant nature. To date, 30 cases of immature teratoma have been reported in the literature [1, 3–15]. Herein, we report on the clinicopathologic findings of an infant with down syndrome who presented with hematemesis and severe anemia. Finally, he was diagnosed with immature gastric teratoma.

Case Report
An 8-month-old patient presented with hematemesis and anemia of one-month duration. He had an underlying disease of down syndrome and congenital hypothyroidism. Physical examination of abdomen showed an enlarged, intra-abdominal mass, predominantly in the left upper quadrant of abdomen. Relevant laboratory data included a hemoglobin of 2.4 g/dL, hematocrit 9.8%, and white blood cell count of 14,220 cells/mm³. Anti-HIV was nonreactive by enzyme-linked immunosorbent assay (ELISA). Plain abdominal radiograph showed a soft tissue density in the left upper quadrant of abdomen. Endoscopic gastroduodenoscope was performed and revealed a large intragastric soft tissue mass with ulcer (Fig. 1A and B). An incisional punch biopsy of the mass was performed. He underwent a single-phase venous scan computed tomography (CT) of the whole abdomen that revealed an endophytic heterogeneous hyperattenuating soft tissue mass measuring 7.4 × 6.9 × 4.9 cm, located in the stomach and protruding from the lesser curvature. Small areas of punctuated calcification and a small focal area of macroscopic fat were also observed. The incisional biopsy showed immature myeloid cells infiltration, compatible with granulocytic sarcoma. The bone marrow
biopsy showed active trilineage hematopoiesis without evidence of malignancy. He received two cycles of chemotherapy including cytosine arabinosine 2.5 mg/kg/day for 7 days and idarubicin 0.25 mg/kg/day for 3 days. The gastric mass was progressively enlarged. Abdominal CT revealed a huge heterogenous enlarge gastric mass measuring 11.8 x 10.5 x 4.7 cm. (Fig. 2). The mass increased in size with internal calcification and

Figure 1. The gastroscope shows an endophytic soft tissue mass locating within the stomach (A, B). The gross section shows an endophytic well-circumscribed rubbery firm red-brown mass measuring 13 x 11 x 6.5 cm, originating from the lesser curvature (C). The cut surfaces of mass revealed a solid-cystic and gelatinous appearance with focal cartilaginous and pigmented areas (D).

Figure 2. Coronal CT scan of the whole abdomen before, during, and after chemotherapy shows markedly increased size of the mass within 2 months with increased internal calcification and fat components.
intratumoral fat component. In addition to an increase in size, he developed upper gastrointestinal bleeding which required blood transfusion. Subsequently, he underwent near-total gastrectomy. Laboratory investigation on admission showed increased serum alpha-fetoprotein (50 ng/mL; reference 0–7.02 ng/mL). The final pathologic diagnosis was immature teratoma, grade I. The AFP level returned to a normal range after complete surgical resection. At the 2 years of follow-up, he remains well and exhibits no evidence of recurrence and systemic metastasis. He has been advised routinely follow-up.

Pathological findings

The resected stomach measuring 15 × 11 × 7 cm showed an endophytic well-circumscribed rubbery firm red-brown mass measuring 13 × 11 × 6.5 cm, originating from the lesser curvature (Fig. 1C). The cut surfaces of mass revealed a solid-cystic appearance with focal cartilaginous, gelatinous, and pigmented areas (Fig. 1D). The histopathology revealed various types of tissues including skin, respiratory epithelium, adipose, cartilage, bone, muscle, brain, uvea, choroid plexus, and focal immature germ cell component including neural tube and immature cartilage. Focal extramedullary hematopoiesis was observed (Fig. 3). The tumor invaded mucosa and submucosa without involvement of muscularis propria. Angiolympathic invasion was not detected. The tumor was completely excised. The final pathologic diagnosis was immature gastric teratoma, grade I Table 1.

Discussion

Teratoma originates from the precursor totipotential stem cells and is the most common germ cell tumor in children. It can be either gonadal or extragonadal tissue in origin. The extragonadal teratoma is usually found in younger children, whereas the gonadal tumor is often diagnosed in the older ones [2]. The sites of extragonadal teratoma are sacrococcygeal (60–65%), mediastinal (5–10%), sacral (5%), and rarely intracranial, retroperitoneal, cervical, and alimentary [8]. Gastric teratoma is uncommon, contributes less than 1% among teratoma in pediatric patients [1]. Moreover, immature gastric teratoma is relatively rare. There are thirty reported cases in the literature [1, 3–15]. The age at presentation occurs principally during infants and young children. The reported ages of patients range from birth to children with 4-year-old with a mean age of 4.1-month-old [1, 3–15]. One-fifth of cases have been described at birth [1, 5, 6, 13]. Immature gastric teratoma occurs mostly in boys; only two cases have been reported in girls (6.7%) [1, 15]. The tumor size ranges from 4 to 23 cm with a mean and median size of 12 cm in greatest dimension [1, 3–15]. The most frequent clinical presenting symptoms are abdominal distension, palpable mass, and vomiting [1, 3–15]. Moreover, upper

Figure 3. The histopathology shows various types of tissues including skin, respiratory epithelium (A), adipose, cartilage, bone (B), muscle, brain, uvea (C), choroid plexus (D), and focal immature germ cell component including neural tube (E) and immature cartilage. Focal extramedullary hematopoiesis is observed (F).
| Reference                  | Year   | Age     | Sex | AFP level (ng/mL) | Tumor size (cm) | Location                        | Histologic grade | Treatment                      | Follow-up duration (months) | Outcomes                          |
|----------------------------|--------|---------|-----|------------------|-----------------|---------------------------------|------------------|---------------------------------|------------------------------|----------------------------------|
| Falik-Borenstein et al.    | 1991   | Congenital | M   | NA               | 9.5             | NA                              | 2                | Complete excision               | 4                            | No recurrence                     |
| Muñoz et al.               | 1992   | 45 days | M   | NA               | 12              | Anterior gastric wall           | 1 at least       | Complete excision               | 96                           | No recurrence                     |
| Gengler et al.             | 1995   | 1 month | F   | NA               | 9               | Posterior gastric wall          | 1 at least       | Complete excision               | NA                           | No recurrence                     |
| Sarin et al.               | 1997   | 45 days | M   | NA               | 10              | Greater curvature               | 1 at least       | Complete excision               | 5                            | Recurrence and death              |
| Ratan et al.               | 1999   | 6 months | M   | Normal           | 18              | Posterior gastric wall          | 3                | Complete excision               | 6                            | No recurrence                     |
| Chandrasekharam et al.     | 2000   | 5 months | M   | NA               | NA              | NA                              | 1 at least       | Complete excision               | 12                           | No recurrence                     |
| Gupta et al.               | 2000   | 6 months | M   | 100              | Large           | Lesser curvature, liver,       | 3                | Complete excision               | 18                           | No recurrence                     |
|                           |        | 3 months | M   | 1750             | Large           | Posterior gastric wall,         | 3                | Complete excision               | 4                            | No recurrence                     |
| Yoon et al.                | 2000   | 3 months | M   | NA               | 14              | Greater curvature               | 1 at least       | Complete excision               | 3                            | No recurrence                     |
| Utsch et al.               | 2002   | Congenital | M   | 33,456           | 10              | Greater curvature               | 2                | Complete excision               | 16                           | No recurrence                     |
| Park et al.                | 2002   | Congenital | M   | 33,456           | 10              | Greater curvature               | 2                | Complete excision               | 30                           | No recurrence                     |
| Wakhlu et al.              | 2002   | 4 years | M   | Normal           | Massive         | Posterior gastric wall          | 1 at least       | Complete excision               | 24                           | No recurrence                     |
| Hook et al.                | 2003   | 25 days | M   | Normal           | 9.5             | Posterior gastric wall          | 3                | Complete excision               | 6                            | No recurrence                     |
| Saleem et al.              | 2003   | Congenital | M   | NA               | Massive         | NA                              | 1 at least       | Complete excision               | NA                           | NA                               |
| Corapcioglu et al.         | 2004   | 5 months | M   | 189              | 15              | Lesser curvature                | 2                | Complete excision and chemotherapy | 15                           | No recurrence                     |
|                           |        |         |     |                 |                 |                                 |                  |                                 |                              |                                   |
| Ukiyama et al.             | 2005   | 4 days  | M   | 80,050           | 5.5             | Lesser curvature                | 1 at least       | Incomplete excision             | 24                           | Recurrence                       |
| Bhat et al.                | 2007   | 7 months | M   | 154              | 8.5             | Greater curvature               | 2–3              | Complete excision               | NA                           | NA                               |
| Yadav et al.               | 2007   | NA      | NA  | NA               | NA              | NA                              | NA               | NA                              | NA                           | NA                               |
| Herman et al.              | 2008   | Congenital | M   | 47.4             | 13              | Lesser curvature                | 1 at least       | Complete excision               | NA                           | NA                               |
| Akram et al.               | 2009   | Congenital | M   | 255,496         | 10              | Lesser curvature                | 3                | Complete excision               | 9                            | No recurrence                     |
| Bhattacharya et al.        | 2010   | 2 days  | M   | NA               | 8               | Lesser curvature                | 2 at least       | Complete excision               | 24                           | Recurrence with GP and hepatic metastasis |
| Mohta et al.               | 2010   | 20 days | M   | 690              | 6.6             | Anterior gastric wall           | 1 at least       | Complete excision and chemotherapy | 6                            | No recurrence                     |
| Sharif et al.              | 2010   | 45 days | M   | 110              | Huge             | Posterior gastric wall          | 3                | Complete excision               | 6                            | No recurrence                     |
| Sharma et al.              | 2010   | 5 months | M   | NA               | 15              | Posterior gastric wall          | 3                | Complete excision               | NA                           | NA                               |
| Valenzuela-Ramos et al.    | 2010   | 6 months | M   | Normal           | 4               | Lesser curvature                | 1 at least       | Complete excision               | 36                           | No recurrence                     |
| Yeo et al.                 | 2010   | 14 days | M   | 352              | 12              | Greater curvature               | 3                | Complete excision               | 7                            | Recurrence with GP               |
| Singh et al.               | 2011   | 4 months | M   | Normal           | 23              | Lesser curvature                | 1                | Complete excision               | 12                           | No recurrence                     |
| Jeong et al.               | 2012   | Congenital | M   | >60,500          | 15.5            | Posterior gastric wall          | 3                | Complete excision               | 0.5                          | No recurrence                     |
| Anikumar et al.            | 2013   | 3 months | M   | Normal           | 15              | Posterior gastric wall          | 3                | Complete excision               | 6                            | No recurrence                     |
| Kumar et al.               | 2013   | 2 months | F   | 54,000           | 20              | Posterior gastric wall          | 3                | Complete excision               | NA                           | NA                               |
| Junhasavasadikul et al.    | Presented case | 8 months | M   | 50               | 13              | Lesser curvature                | 1                | Complete excision               | 12                           | No recurrence                     |

*Original reference cited in reference.
AFP, alpha-fetoprotein; M, male; F, female; NA, not available; GP, gliomatosis peritonei.
Immature gastric teratoma in an infant with down syndrome

T. Junhasavasdikul et al.

Gastrointestinal bleeding has been reported [1]. Gastric teratoma can also cause respiratory distress due to a pressure effect to the diaphragm [13]. The immature gastric teratomas more often originate from the posterior wall and greater curvature of the stomach [1, 3–15] and can be exogastric and endophytic growth in 58–70% and 30%, respectively [12]. Endoscopy and imaging procedures such as radiography, ultrasonogram, and CT may allow early recognition of gastric teratoma.

Radiographic evaluation of gastric teratomas can be differentiated from other common abdominal masses by the presence of associated calcification about 40–60% of all gastric teratomas [12]. The differential diagnoses of plain abdominal radiograph with the left upper quadrant soft tissue mass containing internal calcification include mesoblastic nephroma, nephroblastoma (Wilm tumor), neuroblastoma, ganglioneuroblastoma, ganglioneuroma, and teratoma [12].

Ultrasonography can reveal an internal content of the mass which shows heterogeneous echogenicity, mixed solid-cystic component, and internal calcification [6], but the origin of the mass, especially in the huge one, is hardly demonstrable. Nevertheless, a normal kidney on the ultrasonographic finding can exclude the primary renal tumor.

Computed tomography is more useful in demonstrating the component of mass, its intragastric location, and its extension. Both teratoma and neuroblastic tumor may contain solid and cystic components as well as internal calcification [6, 12]. In our case, however, the presence of gastric invasion and internal fat component favor gastric teratoma while these features are rarely presented in neuroblastic tumor. In conclusion, radiographic findings of the intragastric mass with internal fat component and calcification suggest the diagnosis of the gastric teratoma.

Gastric tumor is an uncommon neoplasm in pediatric patients. Endoscopic evaluation and gastric tissue biopsy must be performed. The more common tumor-mimic lesions including foreign body and bezoars must be initially excluded. The differential diagnoses of gastric tumor include juvenile polyp, hematologic malignancy, gastrointestinal stromal tumor (GIST), smooth muscle tumor, inflammatory myofibroblastic tumor, and teratoma [1]. In our case, the gastric punch biopsy of teratomatous components yielded brown to dark-brown tissue, and histological examination showed that most cellular components were immature myeloid cells, compatible with granulocytic sarcoma. The following gastrectomy specimen showed immature teratoma with extramendillary hematopoiesis. A possible reason for the misdiagnosis in gastric punch biopsy specimen is the interpretation of immature myeloid cells to granulocytic sarcoma, which is found in the area of extramendillary hematopoiesis of immature gastric teratoma. The granulocytic sarcoma made up of immature myeloid cells histologically indistinguishable from that occurring in the extramendillary hematopoiesis. Moreover, individuals with down syndrome have an increased predisposition to acute leukemia, predominantly myeloid type including granulocytic sarcoma. Extramendillary hematopoiesis can be misinterpreted as representing a pathologic or neoplastic process.

Besides awareness and purely histologic criteria, a false-positive identification of immature hematopoietic cells as granulocytic sarcoma may be avoided by the use of immunohistochemical stains for the maturing hematopoietic cells including myeloperoxidase and lysozyme for the granulocytic line, hemoglobin A and glycophorin A for the erythroid line, CD41, CD61, and factor VIII for the megakaryocytic line, which are highlight the extramendillary hematopoietic cells.

Complete surgical resection remains the cornerstone of treatment of gastric teratoma. Immature gastric teratoma has an excellent prognosis after a complete surgical resection. Adjuvant chemotherapy or radiotherapy is not recommended. Follow-up consists of regular observation and serum AFP measurement to monitor for recurrence or malignant transformation. In case with rising AFP level after surgical resection of gastric teratoma, chemotherapy is recommended. Some authors suggest aggressive postoperative chemotherapy to prevent local recurrence, if there is histopathologic evidence of grade III immature teratoma or malignancy demands including nephroblastic elements. However, the role of chemotherapy in immature gastric teratoma is still not explicitly clear, because of the rarity of cases.

Therefore, it is noteworthy to keep gastric teratoma in mind when dealing with mass lesion in the stomach. The biopsy of teratoma can reveal extramendillary hematopoiesis that may simulate hematologic malignancy, and the context of the specific radiologic feature, and index of suspicion should be maintained, tumor marker obtained, and repeat biopsies performed before committing to intensive chemotherapy. Early diagnosis and prompt medical treatment with careful follow-up are essential. Further genetic and molecular investigation is needed to provide pathogenesis of immature gastric teratoma.

Conflict of Interest

The authors declared that there is no conflict of interest.

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