A case of mild congenital hyperinsulinemia presenting with developmental delay, complicated by diazoxide-induced transient neutropenia

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Background

Congenital hyperinsulinemia (CHI) can cause various degrees of hypoglycaemia in infancy. In mild form of CHI, unnoticeable and recurrent hypoglycaemia may cause deterioration of the central neurological functions.

We report a case of mild CHI that presented with seizure and developmental delay without noticeable previous hypoglycaemic events.

Case presentation

An 18-month-old Japanese girl was admitted to our hospital with seizure and unconsciousness. Because her blood glucose levels on admission was rather low in spite of receiving maintenance fluid therapy, we repeated measuring her blood glucose levels and found 40 mg/dL of hypoglycaemia concomitant with serum insulin level of 10.9 μU/mL (Table). On the basis of these findings we made a diagnosis of CHI.

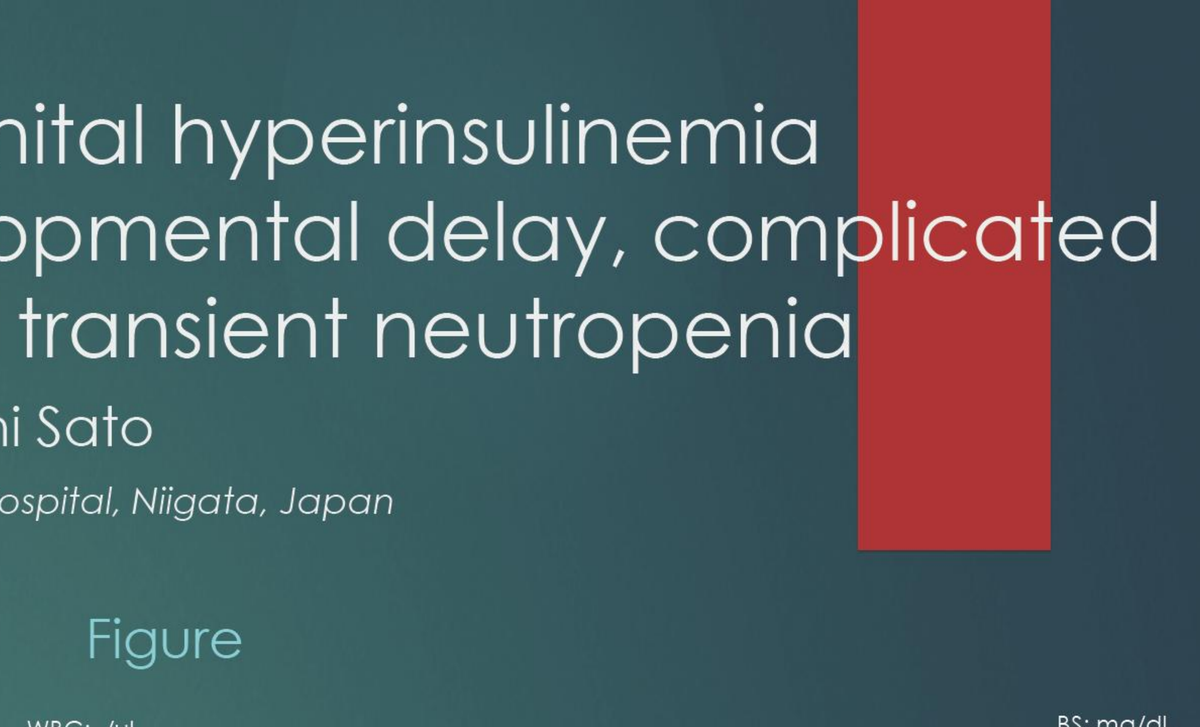
The patient had never shown any apparent hypoglycaemic events previously and had developed normally until 6 months of age. Thereafter, she began to show developmental delay mainly in large movements.

Clinical course

The patient was administered diazoxide ,followed by severe neutropenia of 168 /μL. A bone marrow aspiration performed 2 days after cessation of the drug showed a reduction in nucleated cell count of 6.2×10^4 /μL with increased numbers of immature myeloid cells, indicating transient myeloid suppression.

We were unable to control her blood glucose levels appropriately by meals and other supplemental diets. Furthermore, octreotide is not registered for treatment of CHI in Japan. She was restarted on diazoxide with close monitoring. The patient has not developed neutropenia again and her glycaemic status has been successfully controlled (Figure). she is receiving 8mg/kg/day of diazoxide with normal blood cell count now.

Figure



Discussion

We speculate that relatively frequent milk-feeding during early infancy may have masked her hypoglycaemia. Thereafter, as the feeding interval got longer, unnoticeable and repeated hypoglycaemia may have occurred and caused her neurological deterioration.

There are only few reports of diazoxide-induced neutropenia and limited information is available. The drug was discontinued in all cases and one of them underwent surgical resection of pancreas. However surgical procedure is often complicated by secondary diabetes mellitus. Octreotide is another useful therapeutic option. But daily subcutaneous infusion may be a heavy burden to young children.

Conclusion

In patients who develop gradual central neurological delay, unnoticeable and repeated hypoglycaemia may be the cause. In such cases, recurrent blood glucose measurements should be recommended even if they do not show hypoglycaemic symptoms.

Neutropenia is a rare adverse effect of diazoxide. This may be transient and the drug could be reintroduced with close monitoring after recovery of bone marrow.

Table

Blood glucose	40	mg/dL	Free Fatty Acid	1238	μEQ/L
NH_3	24	μg/dL	3-OH-Butiric Acid	4566	μmol/L
Lactate	9.0	mg/dL	Acetic Acid	1600	μmol/L
Pyruvate	0.74	mg/dL	Total carnitine	33.6	μmol/L
Serum Insulin	10.9	μU/mL	Free carnitine	12.7	μmol/L
Growth Hormone	42	ng/mL	Acyl carnitine	20.9	μmol/L
Cortisol	10.70	μg/dL			

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